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VOLUME XXIV

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CHARLES LYBRAND BONIFIELD

1863-1932

# American Journal of Obstetrics and Gynecology

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VOL. XXIV

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## IN MEMORIAM

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CHARLES LYBRAND BONIFIELD

MARCH 23, 1863—APRIL 23, 1932

IT IS allotted to few men to have so varied a career as the subject of this brief biographical sketch. Born on a farm near Zanesville, Ohio, Dr. Bonifield received his early education in the county schools, then became an assistant to a dentist in a neighboring town for two years. Discouragement served to make him go to Cincinnati, where he entered the Medical College of Ohio, and graduated with the class of 1886. Soon afterward he opened an office at Fourth and John Streets in Cincinnati, where he developed a general practice. Fortune soon smiled upon him, for he had an uncle, Dr. Thaddeus Reamy, a distinguished gynecologist, who took Dr. Bonifield together with Dr. John Withrow as assistants in his office.

When Christ Hospital was opened in Cincinnati, Drs. Withrow and Bonifield were appointed gynecologists with alternating services of six months each. Later on Dr. Bonifield also became identified with the Ohio Medical College and the Good Samaritan Hospital as Dr. Reamy's assistant. Here he had an opportunity to develop his teaching talents both in the out-patient department and in the operating room. His popularity among the students, his marked ability as a teacher and his genial manner soon made him an outstanding figure in the local profession and patients flocked to him in large numbers. Dr. Bonifield finally succeeded Dr. Reamy in the Chair of Gynecology of his Alma Mater, and later was appointed Gynecologist to the Cincinnati General Hospital. Both of these positions he held to the day of his death.

In 1892 he spent a year in Germany perfecting himself in his specialty and was a pupil of Professor Martin. Dr. Bonifield took an active part in the political and civic affairs of Cincinnati and in 1920 was the Democratic candidate for Mayor. Although he was defeated he polled a very large vote.

Dr. Bonifield's long medical career brought him many honors. He was President of the Cincinnati Academy of Medicine, Ohio State Medical

Society and the American Association of Obstetricians, Gynecologists and Abdominal Surgeons. He was likewise a Diplomate certified by the American Board of Obstetricians and Gynecologists and a member of several other professional organizations.

Dr. Bonifield was a hard worker in his specialty; he was also a prolific and vigorous writer and deeply interested in the welfare of his assistants and medical students. He had a strong character, he was fearless and would fight hard for his opinions when he believed that he was in the right.

His portrait hangs in the University Medical School of Cincinnati. It was given to him only a year ago by his many friends at a testimonial dinner.

The subject of this memorial was a member of the Advisory Editorial Board of the AMERICAN JOURNAL OF OBSTETRICS AND GYNECOLOGY since its organization and was always interested in its progress and welfare.

Dr. Bonifield's first wife was Miss Mabel Finney, and following her death some four years later he married her sister, Miss Grace Finney, and to this union two children were born, Mabel and Charles, who survive him.

Dr. Bonifield had been in poor health for the past two years but apparently was on the road to recovery, when a cerebral hemorrhage suddenly cut short the career of this brilliant surgeon and notable citizen.

*Magnus A. Tate.*

## Original Communications

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### THE FOUNDATION OF AN ENDOCRINE CLINIC FOR THE STUDY AND TREATMENT OF AMENORRHEA, UTERINE BLEEDING, AND STERILITY\*

BROOKE M. ANSPACH, M.D., AND JACOB HOFFMAN, M.D.,  
PHILADELPHIA, PA.

*(From the Department of Gynecology, Jefferson Medical College Hospital)*

IT IS becoming more and more apparent that endocrine dysfunction is a frequent cause of menstrual disorders and sterility. We constantly meet with patients who complain of menstrual disturbances, in whom there is no gross lesion in the pelvis. The same statement may be made relative to the female partner in the barren marriage. In a further general study of these two groups one often concludes that none of the usual constitutional diseases are present and then asks whether imbalance of the endocrine glands may be at the bottom of the trouble. Sometimes our attention is turned in this direction by the very obvious stigmas of the endocrinopathies in the individual, and sometimes our attention is turned to the endocrine glands because, so far as we know, we have excluded all other causes.

The patients who complain of these symptoms form a considerable part of the gynecologist's clientele. The need of methods of precision in diagnosis is obvious and a successful plan of treatment is much to be desired. The problems presented are perplexing for what appears to be true one day may be shown to be a fallacy the next. Perhaps the time has arrived when the theories that have been built up may be applied. For that reason we have organized at the Jefferson Medical College Hospital a special clinic to which all endocrine cases are referred. This paper is for the purpose of reviewing the information that is now at hand relative to the influence of the endocrine glands upon the genital function and of appraising the available means of treatment.

We are especially interested in two groups, first, the deficiencies of the menstrual flow, complete or partial and the lowering of the fertility index with which it is often associated, and second, the abnormal bleedings appearing as menorrhagia or metorrhagia in which an exhaustive search for organic lesions in the pelvis has been fruitless.

An outstanding fact which should be mentioned at this point is that

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\*Read at a meeting of the Obstetrical Society of Philadelphia, November 5, 1931.

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NOTE: The Editor accepts no responsibility for the views and statements of authors as published in their "Original Communications."



ovulation may be denied to the woman who bleeds too often and too freely as well as to the woman who has no bleeding from the uterus at all.

We have for a long time associated a lack of uterine bleeding with a lack of ovulation, but only in recent years have we realized that menstruation, or what passes for menstruation, without ovulation may take place. So that what at first sight might appear as *hyper*-function is relegated properly to the domain of *hypo*-function.

The basis of our remarks is the literature upon the subject and our own experience, which of course is much too recent and far too limited for any final estimate. They are presented with misgivings because of the intricacies of endocrinology and the apparently contradictory results of investigation; but we hope that a discussion of these topics will indicate in some measure the value of what has already been learned and lend a good influence in the direction of future work.

The plan of handling endocrine patients that we submit has three objects; first to determine the source and degree of the disturbance; second to apply what appears to be the logical treatment, and third to note the immediate and the late results. Close association of clinical and laboratory methods is of the greatest necessity.

Up to the present time we have treated 40 cases of irregular bleeding with the anterior pituitary luteinizing substance; there were only two failures and in one of them placental tissue was found in the uterus. The use of hormones seems to have less influence upon amenorrhea; we have had but one success in 10 cases; here roentgen-ray stimulation of the anterior pituitary and the ovary may give better results. We have been fortunate enough to obtain our object in 10 out of 30 cases. A detailed study and report of the work in our Endocrine Clinic will be made later.

*Physiology.*—The contributions of Hitschmann and Adler, Schroder, Robert Meyer, Zondek and Aschheim, Smith and Engle, Frank, Allen and Doisy, Corner, and others are responsible for our present knowledge of the functional relationship between the ovary and the uterus, and the modern conception of the physiology of menstruation and reproduction. A brief review of the relation between the more important constituents of the ductless system and the genitalia is as follows:

*Thyroid.*—One of the most prominent indications of an interrelationship between the thyroid and the genital organs is the enlargement of the gland that occurs during pregnancy and menstruation. Disturbances of the thyroid may be responsible for various forms of menstrual disorder, and any of them may be benefitted clinically by thyroid therapy. Patients suffering from Basedow's disease are usually sterile, and pregnancy when it does occur exercises a decidedly unfavorable influence. It has been shown, experimentally, that extirpation of the thyroid in young animals results in high grade genital infantilism; the ovaries exhibit degenerative changes and follicular atresia. Extirpation in the full-grown affects fertility and milk secretion.

*Anterior Pituitary.*—The anterior lobe of the pituitary initiates ovarian function during adolescence and maintains it from puberty to the menopause. It pro-

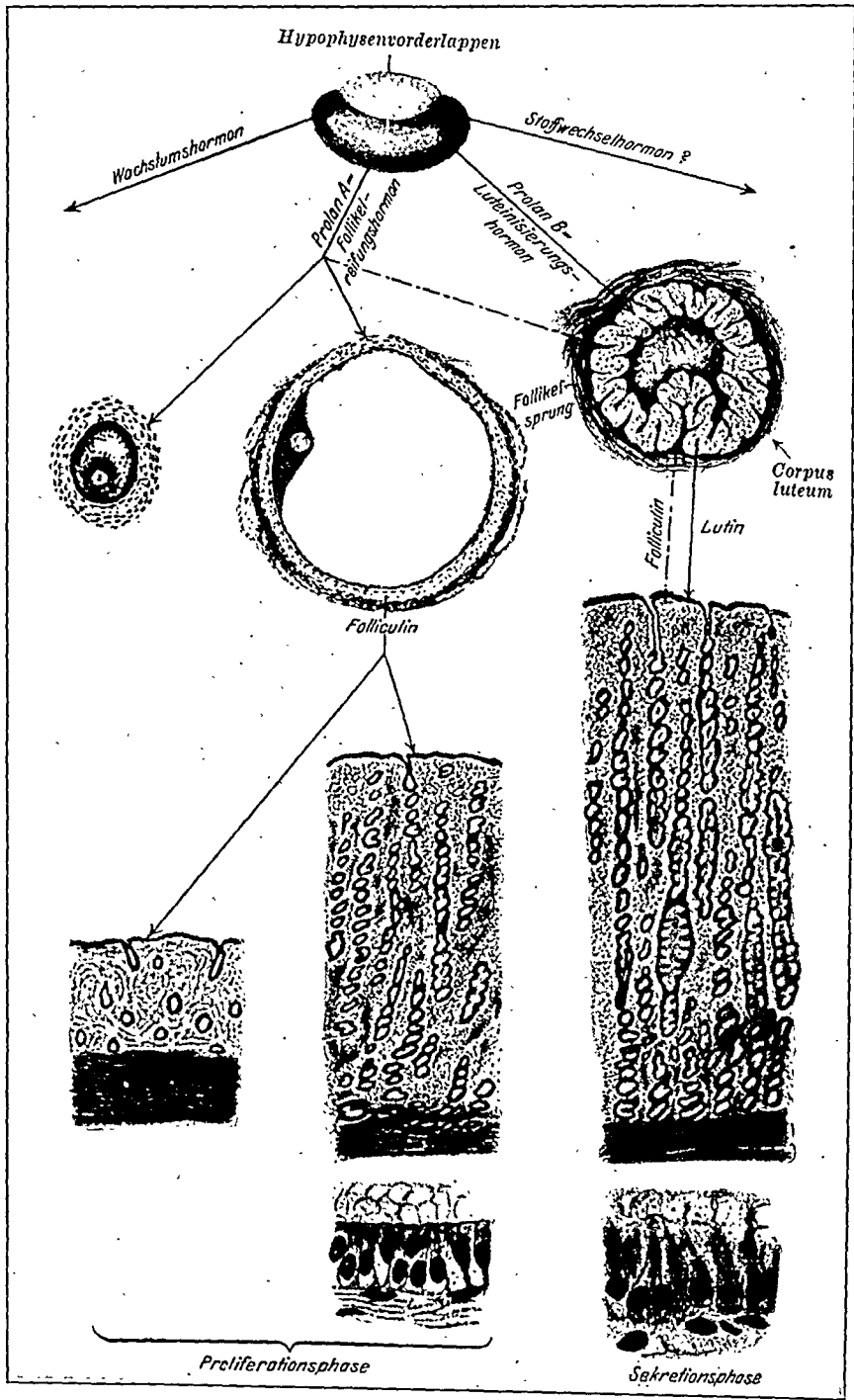


Fig. 1.—Anterior pituitary gland and genital function in the female (after Zondek).

duces several powerful hormones, of which some influence general somatic growth and metabolism, and others, the generative organs. The anterior pituitary sex hormones, are known as Prolan A and Prolan B. Prolan A brings about follicular maturity and egg-ripening. Prolan B supplements Prolan A and causes luteinization of mature follicles and corpus luteum formation. It is believed that when the ovum is not fertilized Prolan B is withdrawn, the corpus luteum degenerates and menstruation ensues. When conception occurs, Prolan B continues its action, the corpus luteum grows larger and continues to function.

*Ovary.*—The ovary under the influence of the anterior pituitary manufactures a follicular hormone and a lutein hormone.

*Control of Endometrium by Pituitary and Ovarian Hormones.*—The action of the anterior pituitary and of the ovarian hormones upon the mucosa of the uterus preparatory to menstruation and after conception is of practical importance, for the reason as will be shown later that normal changes in the mucosa of the uterus indicate normal function of the ovary itself and of the glands that govern it. The examination of curettings in menstrual disorders and in sterility is therefore of much diagnostic importance. It is possible to distinguish: the atrophic mucosa which means that there is no follicular hormone; the interval mucosa which signifies a normal amount; the hyperplastic mucosa which may indicate an excess, and the premenstrual mucosa which manifests both follicular and lutein hormone in balanced proportions. The endometrial picture gives us a reliable index of the ovarian function (Fig. 1).

It must not be forgotten however that uterine bleeding simulating menstruation possibly may occur in some women without ovulation and premenstrual changes in the endometrium, as has been demonstrated in the monkey by Corner. This phenomenon may be spoken of as menstruation without ovulation and has never been explained.

The application of our knowledge relative to physiology is a very important factor in the diagnosis and treatment of the endocrine disorders of the reproductive system. We may include here also certain forms of dysmenorrhea and the annoying vasomotor disturbances of the artificial and the natural menopause. The study of the individual patient includes a search for a predisposition to endocrine disturbances; a complete physical examination, general endocrine studies such as an x-ray of the sella turcica, sugar tolerance and basal metabolism tests, investigation of the autonomic nervous system (flushes, local sweats, erythematous eruptions, and tremors), estimation of the blood pressure and examination of the eye-grounds; observation of the stature, coloring, spacing of the teeth, shape of the fingers, quality of the voice, hair, and fat distribution, the development of the pelvic bones, the pelvic organs and the secondary sexual characteristics.

Of especial importance is an examination of the blood and the urine for ovarian and anterior pituitary hormones. The tests we use here are those of Frank and Goldberger for the follicular hormone and those of Zondek for the anterior pituitary hormone. According to Frank, the follicular hormone test divides patients into three groups, viz.: those with what may be considered a normal reaction, those with less than the normal reaction—subthreshold cases, and those with no reaction at all.

While Frank and Goldberger's test is of importance in estimating

the ovarian function, it is to be remembered that a normal reaction or a polyhormonal state does not signify full ovarian function or luteinization of the follicles; the only way of determining the presence of lutein or progesterin is by an examination of endometrial curettings for the premenstrual stage.

The demonstration of the anterior pituitary hormone in the blood or the urine is never possible in the normal nonpregnant woman; its presence is taken as an index of ovarian failure, an assumption based on the fact that it appears in the blood and the urine during the last stage of the menopause and following castration.

By means of these blood and urine tests and by examination of the uterine mucosa, we aim to arrive at a fair estimate of the functional deficiencies of a given case.

#### CLINICAL DIVISION OF ENDOCRINE SUBJECTS

We may group patients suffering with endocrine disorders according to the leading symptoms or according to the gland chiefly affected. Functional disorders of menstruation may be primary, appearing at puberty or they may be secondary, arising later in life. Sterility may be the outstanding feature and dwarf all other complaints. According to the gland that chiefly seems to be at fault we may list them as ovarian, pituitary or thyroid endocrinopathies. Each has certain features of diagnostic importance.

In dealing with the ovarian group, many authors in the past have spoken of the hyper- and the hypoovarian state, basing this division upon the character of the menstrual flow and more recently upon the female sex hormone content of the blood and urine. That such assumptions may not be true is shown by the work of Zondek that a polyhormonal state is found sometimes in amenorrhoeic women as well as in the early menopause. We should like to draw attention at this point to the question already suggested by Keller and Schickele, as to whether amenorrhoea, oligomenorrhoea, menorrhagia, and metrorrhagia may not be of the same genetic origin, and whether they may not be symptoms of a hypoovarian state, either primary, or secondary to pituitary dysfunction.

In explanation of what happens in these pseudohyperactive cases it has been said that follicular atresia takes place at various stages of the follicles' development, either because there is a lack of anterior pituitary hormone or because there is a mechanical obstruction to rupture of the follicle, as for example, a thickened tunica albuginea. The process is repeated until there are present in the ovary a number of atretic follicles, each containing a certain amount of follicular hormone, which stimulates the endometrium and brings it to the intermenstrual phase. But the follicle does not rupture, corpus luteum formation does not take place, the endometrium deprived of a lutein hormone does not reach the premenstrual phase and menstruation does not ensue. Later the en-

dometrium becomes thickened and hyperplastic as a result of continued stimulation by the follicular hormones. Finally, due to an accidental mechanical break in the hypertrophied mucosa or possibly to a chance corpus luteum formation from the gradual accumulation of luteinizing hormone, excessive bleeding begins and continues over a long period of time.

Here, it will be noted, there is first amenorrhea and then menorrhagia from the same basic cause, i. e., a failure in complete ovarian function; and in either instance a large amount of follicular hormone produced in the atretic follicles is found in the blood. Before one can be sure that a large amount of follicular hormone in the blood is indicative of full ovarian function, one must find the endometrium in the premenstrual stage. Paradoxical though it may seem, menorrhagia and an excess of follicular hormone sometimes must be ascribed to a failure rather than to an increase of ovarian function.

There is no evidence of the occurrence of a state of hyperfunction of the *anterior pituitary* in the manufacture of sex hormone, except the fact that tumors of the pituitary are associated with sexual precocity.

Hyperfunction of the *thyroid* of course is frequently demonstrable. Abnormal thyroid function is diagnosed more readily than the abnormal function of other glands; because the symptoms are more evident and the rate of basal metabolism is a more or less accurate index. Medication for a deficiency or an increase of function of the thyroid is readily applied and often prompt in its effect.

#### TREATMENT OF ABNORMAL ENDOCRINE FUNCTION

It is reasonable to suppose that success in the treatment of endocrine disorders depends upon an accurate diagnosis as to what is wrong and upon the efficiency of the means at hand to correct it. We have seen already that abnormal function of the ovary is principally in the direction of too little function rather than too much, and that as the pituitary, to a large extent, controls the activity of the ovary, it is often the seat of the primary deficiency. In some cases the thyroid plays a part. We may theorize also that the ovary in spite of the usual amount of pituitary and thyroid stimulation is not able to respond in a normal way. Our most difficult therapeutic objective is to stimulate the endocrine glands and so increase their function. Then we may also and perhaps at the same time introduce into the patient quantities of the hormones which she lacks, taken from the urine of pregnant animals. This is therapy by substitution pure and simple but in the end it may prove to be stimulative and set the normal function going. We furthermore may employ agents that so influence the local condition of the affected gland that its normal function may be restored. Here we have the x-ray as applied to the pituitary and the ovary and the vigorous palpation or the surgical treatment of cystic ovaries.

## PROGNOSIS

In addition to the results of the hormone tests and the examination of the endometrium, the age of the patient and the severity and duration of the symptoms are of importance; in the young person we may have an endocrine apparatus that is basically deficient and one therefore that is most difficult to influence while in the older woman whose hypofunction is secondary there may be some chance at least of reviving the former activity.

## MECHANICAL TREATMENT

The purpose of the mechanical method of treatment is to get rid of atretic follicles, retention cysts, and persistent corpora lutea which are impediments to egg-ripening and ovulation. Its object is often effected by repeated bimanual palpation of the ovaries, manipulating them between the fingers so as to exert a certain amount of pressure. Following such manipulation troublesome amenorrhea and menorrhagia may be corrected and a period of sterility may be terminated. We employ this method when the endometrium is hyperplastic. Reynolds and McComber and Meaker advise conservative surgery, viz., excision of the atretic follicles and retention cysts and the liberation of adhesions. It is interesting to speculate that the improvement in the menstrual flow sometimes noted in the newly married may be due to the rupture of atretic follicles as the result of coitus.

## HORMONE TREATMENT

It is important before administering any hormone to make sure with blood and urine studies that there is a deficiency of that particular hormone. The hormone must be given in adequate dose, preferably by intramuscular injection and for a sufficient length of time. Adequate dosage is usually demonstrated by recovery of the hormone in the urine.

The hormonal preparations now available, are those of the ovary and the anterior pituitary. Folliculin, progynon and theelin are among the most potent of the ovarian preparations and the ones in common use. The follicular hormones must be administered always during the first part of the cycle, when their effect is physiologically needed; never when a polyfolliculin state exists, whether manifested by amenorrhea or menorrhagia.

Progesterin, a hormone from the corpus luteum, isolated by Corner and Allen is not yet available for administration to the human. It gives promise of a great step forward in our therapeutics, because lutein hormone is so frequently lacking in endocrine cases. We have been fortunate\* in securing a supply of anterior pituitary luteinizing substance, which corresponds to the Prolan B factor used by Zondek. By administering the follicular hormone during the first part of the cycle and the luteinizing hormone at the middle of the cycle, following the lead of

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\*Through the courtesy of Parke, Davis & Co.

Novak and Hurd, who report 51 cases, we have been able to secure results heretofore denied.

In our small experience this luteinizing hormone has proved of distinct value in checking excessive bleeding in young women at puberty and later; but whether the results will be permanent we do not know.

Use of the ovarian hormone is indicated also in cases in which there is a disturbance of the vegetative nervous system, due to an ovarian insufficiency following ovarian ablation or the natural menopause, except when a polyhormonal stage exists. In the natural menopause there appears to be three stages. First, the polyfolliculin stage, ovarian hormone is contraindicated; second, the oligofolliculin stage, here ovarian hormone may help; third, the polyprolan stage, when both follicular hormone and x-ray treatment of the pituitary are required. In the artificial menopause, the first or the polyfolliculin stage does not occur.

The anterior pituitary preparations, although still in their infancy, offer the greatest possibilities for the future, because unlike the follicular hormones, which are purely substitutive and transient in their effect, the pituitary substance produces definite stimulation. One of us has demonstrated the possibility of rejuvenating the ovaries of senile mice by means of anterior hypophysial implants. The effect was prolonged for several months. If we are to judge from the effect of the experimental implants of fresh gland upon the senile mouse, it is not unreasonable to believe that a preparation potent enough to produce a physiologic stimulus relatively as powerful would be of the greatest aid in combating incipient genital hypoplasia and retardation of the secondary sexual characteristics in the human being for which, as yet, so little has been done. It is reasonable to assume that many obstinate cases of amenorrhea and sterility from underlying pituitary deficiency will benefit by a potent extract. The few preparations on the market are not very satisfactory and are too expensive for practical application. The anterior pituitary luteinizing hormone which is akin to Prolan B we have used with success as noted above.

Thyroid preparations constitute one of the most important and reliable aids in gynecologic endocrinology and are of special value in sterility associated with obesity, amenorrhea and a low basal metabolic rate.

#### ROENTGEN-RAY THERAPY

The judicious use of stimulating doses of roentgen ray, applied to the pituitary, ovary and other endocrine glands, seems to be a valuable agent in combating certain of the functional gynecologic disorders. The course of action of the roentgen ray upon the endocrine glands is still a matter of conjecture. Some think irradiation brings about hyperemia and increased vascularization with intracellular changes in the functioning cells, and a consequent increase in their function. Others believe that

the roentgen ray indirectly stimulates the hormone producing cells by a degeneration of the surrounding cells, and a destruction of their inhibitory influence. The dose varies with the case and depends upon the age, the duration of the disturbance and its severity and the functional status of the gland under consideration. As yet, there is no standard dose. A minute dose stimulates function, a moderate dose strengthens function, a large dose inhibits function, a very large dose destroys function (Arndt-Schmidt).

It is only prudent to reserve irradiation for those cases in which all other forms of treatment have been tried without success. Complete hormonal and endometrial studies must precede its use. In choosing between the pituitary and the ovary as the object of treatment, the pituitary gland should be exposed first in all women during the reproductive period, but especially in young women.

Stimulating doses directed to the hypophysis have been effective in the treatment of amenorrhea, menorrhagia, dysmenorrhea and sterility. The roentgen ray in larger dose has been of value in combating the vasomotor symptoms of the artificial and physiologic menopause, these symptoms apparently depending upon a hyperactivity of the hypophysis, that occurs when there is no longer an *antagonistic* ovarian hormone. In cases of functional uterine bleeding during the menopause (a condition often associated with follicular atresia and endometrial hyperplasia), the roentgen ray in large dose has been administered to both the pituitary and the ovary, there being no longer any fear of damage to the follicular apparatus. The value of pituitary irradiation in incipient or threatened genital hypoplasia has as yet not been ascertained and its usefulness in that direction is an interesting problem.

Ovarian irradiation also either in conjunction with or following pituitary irradiation, must be given in very small dose and over an extended period, because the possibility of germinal injury, especially during the reproductive period, must always be taken into account. While most observers believe that such injurious effects will not occur if the treatment is selected and given properly, it is wise notwithstanding, to consider even the remote possibility of damage and proceed with caution. Where there is a demonstrable amount of pituitary hormone in the blood, indicating ovarian failure it is contraindicated. Irradiation, here may permanently destroy the already hypofunctioning follicular apparatus. The follicular hormone content of the blood is an index of the propriety of treatment, and the roentgen ray should never be used when repeated examinations for the hormone, during a period of five weeks, gives a negative reaction. In subthreshold cases it may be tried in very small doses and with great caution, for here we are dealing with a weakened follicular apparatus and a large dose may do irreparable damage.

There ought to be close cooperation between the gynecologist and the roentgenologist, and both should be alive to the needs of the situation.



Irradiation may be used with success in the treatment of functional sterility (Rubin). Normal menstrual periodicity has been restored, and conception has been attained. Many observers, notably Rubin, report encouraging results. It is advisable to combine the use of the glandular therapy described with the roentgen ray in such cases.

#### CONCLUSIONS

1. A useful purpose may be served by endocrine clinics for the study of the diagnosis and treatment of functional gynecologic disorders, in accordance with the newer ideas relative to the physiology of reproduction.

2. The anterior pituitary and the follicular hormone tests are important diagnostic aids in estimating ovarian function.

3. The picture presented by the endometrium, has proved the most important single observation in estimating ovarian function.

4. The demonstration of anterior pituitary hormone in the blood and urine seems to be a reliable indication of primary ovarian failure.

5. A positive follicular hormone test is not an invariable index of full ovarian activity, since large amounts of this hormone may be found in some cases of amenorrhea and during the first stage of the natural menopause. A negative reaction however is an accurate index of follicular inactivity.

6. The administration of a potent ovarian and pituitary preparation, at the proper phases of the cycle gives promise of value and may be a step forward in the treatment of menstrual irregularities and sterility.

7. What we need most is a more potent anterior pituitary extract.

8. Thyroid products remain as possibly one of the most reliable and potent preparations at our command today and should always be tried when the basal metabolism is low.

9. The roentgen ray, when judiciously applied, seems to be an important therapeutic agent in combating endocrine dysfunction with its associated manifestations.

## THE CARDIAC OUTPUT IN PREGNANT WOMEN

H. J. STANDER, M.D., AND J. F. CADDEN, BALTIMORE, MD.

*(From the Department of Obstetrics, Johns Hopkins Hospital and University)*

THE question of the strain of pregnancy, especially on the diseased or damaged heart, is of importance. The correct procedure in handling a pregnant patient suffering from heart disease depends not only on the proper evaluation of the particular cardiac lesion and the quality of the heart musculature, but also on a knowledge of the amount of additional work placed upon the heart as a result of pregnancy, labor, and the puerperium.

That normal pregnancy is accompanied by a steady and progressive increase in heart output as term is approached, is suspected from the increase in body weight, total blood volume and the marked hypertrophy of the uterus and its adnexa. During the latter half of her pregnancy the normal woman often shows slight signs of cardiac embarrassment as evidenced by shortness of breath on slight exertion.

In 1926 Stander, Duncan, and Sisson<sup>1</sup> reported studies on the heart output in nonpregnant and pregnant dogs. They employed the direct method, based on the Fick<sup>2</sup> principle, later elaborated by Zuntz<sup>3</sup> according to which the minute volume of the heart (M. V.) may be expressed by equation:

$$M. V. = \frac{O}{A - V}$$

where O = total oxygen in c.c. used per minute; A = c.c. of oxygen in 1 c.c. of arterial blood, and V = c.c. of oxygen in 1 c.c. of venous blood. Their results showed that during pregnancy the minute volume of the heart is markedly increased, being one-third to one-half greater than before, and that following labor the minute volume gradually falls and regains its nonpregnant value within two to three weeks.

Since that time Marshall and Grollman<sup>4</sup> have developed a method for determining the cardiac output directly upon man. The various methods for measuring the heart output in man consist either in an application of the Fick principle or in determining the rate of exchange of a normally present gas, such as nitrogen, during the passage of the blood through the lungs. Marshall and Grollman have criticized the carbon dioxide methods, based on the Fick principle, the ethyl iodide procedure as well as the use of nitrogen. The work of these investigators on the heart output in man eventually culminated in the development of the use of acetylene in a direct procedure. This method is based on the measurement of the rate at which acetylene gas is absorbed during the passage of blood through the lungs. Grollman<sup>5</sup> has shown that with this procedure consecutive determinations on the same individual varied only 2 per cent in the values of the cardiac output, an agreement never obtained by any method applied to man.

In this present study we have used the acetylene method of Marshall and Grollman. The oxygen consumption of the subject is first determined by means of a McKesson metabolizer. The subject then breathes deeply and rapidly into a three liter rubber bag containing about 700 c.c.

acetylene and 1800 c.c. of air, and attached to a three-way tap. At the end of eighteen seconds the first specimen of gas is taken in an evacuated tube, and the final specimen seven seconds later. The two gas samples are analyzed for  $\text{CO}_2$ ,  $\text{O}_2$  and  $\text{C}_2\text{H}_2$ . The arteriovenous oxygen difference ( $A - V$ ) is calculated as follows:

$$A - V = \frac{(\text{O}_2) \text{ Dif.}}{(\text{C}_2\text{H}_2) \text{ Dif.}} \times 740 \times \frac{B - 48.1}{760} \times \frac{(\text{C}_2\text{H}_2) \text{ Av.}}{100},$$

where  $(\text{O}_2) \text{ Dif.}$  is the corrected difference in the oxygen and  $(\text{C}_2\text{H}_2) \text{ Dif.}$  that of the acetylene expressed as percentages, while  $(\text{C}_2\text{H}_2) \text{ Av.}$  is the average corrected percentage in acetylene in the two samples, and  $B$  the barometric reading in millimeters of mercury. Combining the numerical terms, we may express the arteriovenous difference by the following equation:

$$A - V = 0.00974 \times \frac{(\text{O}_2) \text{ Dif.}}{(\text{C}_2\text{H}_2) \text{ Dif.}} \times (\text{C}_2\text{H}_2) \text{ Av.} \times (B - 48.1)$$

The minute volume ( $M. V.$ ) of the heart may then be calculated as follows:

$$M. V. = \frac{\text{O}_2 \text{ consumption}}{A - V},$$

where the  $\text{O}_2$  consumption has been corrected to normal temperature and pressure.

We have studied 17 pregnant women throughout the course of pregnancy as well as during the first month of the puerperium. These patients were brought into the hospital once a month for cardiac output determinations. They were admitted to the ward the night before the day of the test. The next morning they were given a light breakfast at six o'clock, and at nine o'clock were placed in a wheel chair in a quiet room. They remained in the chair for two hours, being instructed to keep as quiet as possible. At 11 o'clock their oxygen consumption is determined, followed immediately by rebreathing into the rubber bag containing the acetylene mixture. The test, therefore, was always carried out five hours after eating, and following two hours of complete rest. In selecting the subjects for experimentation an endeavor was made to utilize patients with enough intelligence to successfully cooperate in the procedure.

All gas analyses were carried out in duplicate in a gas analysis apparatus with a carbon dioxide, an oxygen and an acetylene absorber. The carbon dioxide was first determined by absorption in alkali, after which the acetylene was measured by absorption in alkaline mercuric cyanide. Finally the oxygen was determined by absorption in pyrogallol. We used an 11 c.c. pipette which gives an error not exceeding 2 per cent in the final results. In the preparation of the absorbing solutions we followed the instructions of Grollman.<sup>5</sup>

Before applying the acetylene method to patients, we repeatedly determined the heart output of one of ourselves until our technic had been perfected to the extent that the greatest variations in the minute volume were within  $\pm 0.3$  liters per square meter of body surface. We found the heart volume in normal man to be  $2.2 \pm 0.3$ , liters per square meter per minute, which agrees with the figures of Marshall and Grollman.

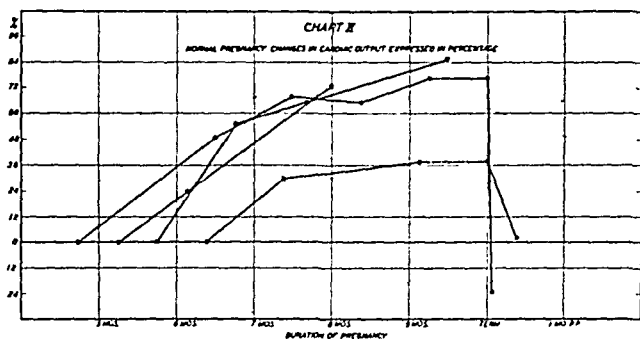
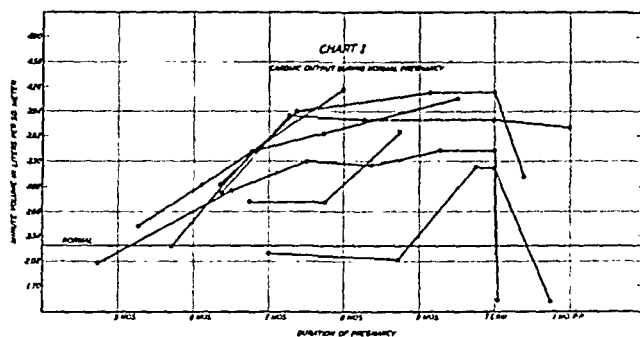
## RESULTS

In Table I we report the weight, the oxygen consumption per minute, the arteriovenous difference in oxygen, the total minute volume, and the minute volume per square meter of body surface at various periods during pregnancy and early puerperium in 13 normal women. From a study of Table I, it will be seen that the heart output in normal pregnant

TABLE I. NORMAL PREGNANCY

CASE	WEIGHT	DURATION OF PREGNANCY	O <sub>2</sub> CONSUMPTION	A-V	TOTAL M.V.	M.V. PER SQ. M.
1	116	6 mo. 1½ wk.	223	49.4	4.5	3.04
	120	7 mo. 1½ wk.	240	40.7	5.9	3.94
	124	9 mo. ½ wk.	270	42.7	6.4	4.19
	107	9 days P.P.	276	61.8	4.5	3.10
2	159	5 mo. 3 wk.	220	56.7	3.9	2.21
	166	6 mo. 3 wk.	249	41.0	6.0	3.43
	170	7 mo. 3 wk.	234	35.9	6.5	3.67
	179	9 mo. 2 wk.	251	33.9	7.4	4.09
3	136	6 mo. 1½ wk.	247	50.3	4.7	2.90
	137	7 mo. 1 wk.	226	35.7	6.3	3.89
	138	8 mo. 1 wk.	232	38.2	6.2	3.83
	123	1 month P.P.	239	41.0	5.8	3.74
4	115	5 mo. 1 wk.	227	63.7	3.7	2.45
	121	6 mo. ½ wk.	219	47.1	4.7	3.02
	127	8 mo.	286	37.3	7.7	4.22
5	169	6 mo. 3 wk.	255	50.6	5.0	2.78
	176	7 mo. 3 wk.	271	53.6	5.1	2.77
	178	8 mo. 3 wk.	321	46.6	6.9	3.69
6	132	4 mo. 3 wk.	215	70.5	3.1	1.97
	140	6 mo. 2 wk.	216	44.8	4.8	2.94
	148	7 mo. 2 wk.	224	40.6	5.5	3.30
	150	8 mo. ½ wk.	240	44.2	5.4	3.24
	154	9 mo. 1 wk.	240	41.0	5.9	3.44
	139	1 day P.P.	203	82.0	2.5	1.52
7	158	7 mo.	216	57.7	3.8	2.12
	168	8 mo. 3 wk.	260	70.1	3.7	2.04
	172	9 mo. 3 wk.	267	44.8	6.0	3.24
	158	3 wk. P.P.	212	76.4	2.7	1.52
8	140	9 mo. 2 wk.	288	40.6	7.1	4.47
9	161	Term	316	35.1	9.0	5.24
10	129	15 days P.P.	199	60.0	3.3	2.06
11	148	Term	299	44.3	6.8	3.97
12	121	6 mo.	226	76.0	3.0	1.94
13	123	4 mo.	192	57.1	3.4	2.20

women steadily increases as pregnancy progresses. This holds strikingly true for 6 out of the 7 patients whom we were able to follow from the end of the third month to full term. The results on these 7 normal pregnant women (Cases 1 to 7 inclusive) are also plotted on Chart I. In this and the other charts we have used 2.2 liters per square meter per minute as the normal level for the heart output and have compared all values to this standard. Each curve in Chart 1 represents the changes in the cardiac output of an individual patient studied at different times throughout the course of pregnancy. It will be seen that the seven curves follow rather closely the same general variations, and this becomes far more apparent when these variations are expressed as changes from a



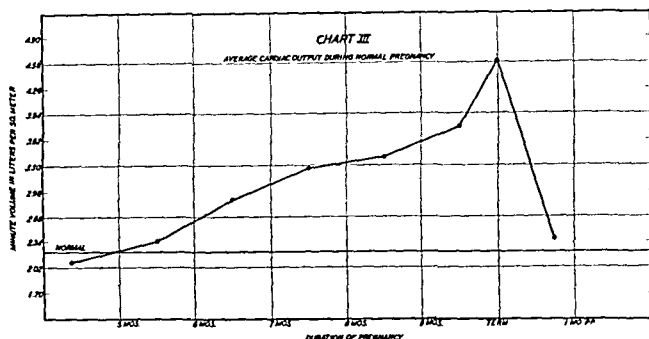
given value, as is shown in Chart II. In this chart the heart output, of each patient at the fourth month, is plotted on a base line, and the variations thereafter are expressed in percentages of this base line value. The curves in this chart are almost identical, showing a steady increase in cardiac output, starting at the fourth month and showing at term an average elevation of about 60 per cent. After delivery the heart output returns to normal at about the third week of the puerperium.

In Chart III we have expressed the average values of all our normal patients at the different months of pregnancy and during the puerperium. These averages are expressed in absolute quantities, being in liters per square meter of body surface per minute. This Chart shows very clearly the steady increase of heart work as pregnancy advances to term. The cardiac output begins to rise above the normal nonpregnant value at about the fourth month of pregnancy, gradually increases until at

term it is 4.58, as compared with the normal of 2.2 liters per square meter per minute. The heart output falls immediately following labor and regains its normal level at the end of the third week of the puerperium.

We attempted to determine the cardiac output during labor, but found that it was impossible to obtain trustworthy results, due to the muscular movements of the patient and the technical difficulties encountered. It is unsafe to draw conclusions from results obtained while the patient moves or performs varying amounts of muscular work.

We have also studied four patients with complications during preg-



nancy. Two of these suffered from heart disease, and two from mild chronic nephritis. The results are reported in Table II. The two cardiac patients, Cases 14 and 15 both show low heart output. Case 14 at term

TABLE II. CARDIAC DISEASE AND NEPHRITIS

CASE	WEIGHT	DURATION OF PREGNANCY	O <sub>2</sub> CONSUMPTION	A-V	TOTAL M.V.	M.V. PER SQ. M.	REMARKS
14	136	Term	203	84.2	2.41	1.66	Cardiac Disease
15	114	7 mo. 2 wk.	114	62.0	3.2	2.15	Cardiac Disease
16	102	4 mo. 3 wk.	221	53.2	4.2	2.96	Nephritis
	108	5 mo. 3 wk.	213	44.6	4.8	3.29	
	112	6 mo. 3 wk.	213	51.3	4.2	2.79	
	122	7 mo. 2½ wk.	232	60.5	3.8	2.47	
	124	8 mo. 2 wk.	234	76.7	3.1	2.02	
	134	9 mo. 1 wk.	269	62.3	4.3	2.67	
17	150	8 mo.	244	60.5	4.0	2.34	Nephritis
	153	9 mo.	255	57.4	4.4	2.56	
	160	Term	222	60.8	3.8	2.21	
	133	9 days P.P.	194	65.6	2.9	1.84	

has a minute volume of only 1.66 liters per square meter as compared with a term value of over 4 liters in normal patients, while Case 15 at seven months' duration showed a heart output of 2.15 liters as compared with normal pregnancy at the seventh month of 3 liters per square meter.

In the two patients suffering from chronic nephritis (Cases 16 and 17), the results are at some variance with the normal pregnancy values.

Case 16 shows an increase in heart output during the first half of gestation, as in normal pregnancy, but undergoes a slight decrease as term is approached. The second patient, Case 17, shows similar changes. The heart output in these two patients suffering from a mild chronic nephritis, reveals the increase seen in normal pregnancy during the first five months, but is not further increased as term is approached. During the puerperium there is a return to normal.

#### DISCUSSION

Our results on cardiac output during normal pregnancy in women are in close agreement with our earlier observations on dogs. Our findings in women show that the cardiac output is increased over one-half during the latter half of pregnancy, and as normal pregnancy is not associated with an appreciable fall in blood pressure, it is apparent that normal gestation is accompanied by a marked increase in cardiac work.

We are at present unable to state whether this additional cardiac work is effected by actual hypertrophy of the heart or by calling into function any reserve force of the heart. Accurate x-ray measurements of the size of the heart in diastole, at different periods of pregnancy, may possibly throw light on this question.

It is evident from the findings reported in this paper that pregnancy requires an increase in cardiac output as early as the fourth month, and that from this time until term the demands on the heart steadily become greater. In the normal woman this demand is evidently met without difficulty. In cardiac patients, on the other hand, the added work induced by pregnancy may be too great a strain on the heart with resulting decompensation and often complete cardiac collapse. The cardiac patient cannot be watched too closely during the course of a pregnancy and labor. If signs of decompensation show soon after the fourth month, the time when pregnancy begins to exert a noticeable demand on the heart, the outlook is grave. In evaluating the heart muscle, the lesion and the type of heart in a pregnant patient with cardiac disease, it is imperative that one constantly bear in mind the ever increasing strain of pregnancy as term is approached as well as the still further demands resulting from labor. We cannot emphasize too strongly that obstetricians should have a correct appreciation of the added cardiac work demanded by pregnancy. Too often does one see pregnancy or labor exert the final overload on a damaged heart with a fatal outcome.

#### CONCLUSIONS

1. The cardiac output in the normal nonpregnant woman is  $2.2 \pm 0.3$  liters per square meter of body surface per minute.
2. In normal pregnancy the cardiac output begins to rise above the normal level at the start of the fourth month.
3. From the fourth month of pregnancy to full term there is a steady

increase in cardiac output amounting to over 50 per cent of the normal value.

4. The heart output slowly returns to normal after delivery and reaches its nonpregnant level by the end of the third week of the puerperium.

5. In pregnant patients with cardiac disease, it is most essential that particular attention be paid to the first appearance of the slightest sign indicating cardiac embarrassment or decompensation, and that in arriving at a proper evaluation of the power of the heart, due recognition to the growing demands of pregnancy be given.

6. Labor undoubtedly produces a still further strain on the heart.

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### BIOCHEMICAL STUDIES OF HUMAN SEMEN\*

#### III. FACTORS AFFECTING MIGRATION OF SPERM THROUGH THE CERVIX

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THE treatment of sterility has yielded only meager results, even in the hands of the most capable gynecologists. The greatest difficulty is experienced with those cases in which one is not able to state, with any degree of certainty, the cause of the sterile marriage. Both husband and wife appear normal in every respect, and yet the marriage remains childless. Either conception has not taken place, or the fertilized ovum has died very early.<sup>1</sup> A careful consideration of the cases reveals the fact that we know relatively very little as to exactly what happens to the human sperm between the times of insemination and fertilization. Deductions drawn from animal physiology concerning this subject and then applied to the human tract are open to very severe and just criticism. We have attempted for the past five years a study of the factors involved in the migration of sperm from the vagina into the tube. It is clear that the physiologic processes involved are very intricate and include numerous biochemical and biophysical factors, and that a failure of any one of these factors may result in sterility.

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<sup>1</sup>One of us (RK) has found in a number of sterile cases a positive Aschheim-Zondek test a day or two after a skipped menstrual period. Menstrual flow, apparently normal in all respects, appeared in each of these cases before the test was completed. Since the test in our hands (on a basis of about 1000 cases) had an accuracy of 98.8 per cent, we feel that these cases were definitely pregnant and that the fertilized ovum had died very early.



The present paper is concerned only with the first step in the sperm migration.

The mechanism by which sperm are directed towards the cervix, and by which they pass through, has been considered by both physiologists and gynecologists. Johannes Müller<sup>10</sup> suggested that semen is forced into the uterine cavity directly at time of ejaculation, by a mechanism simulating the action of a piston in a syringe, the penis acting the part of the piston and the vagina the barrel of the syringe. Lott<sup>9</sup> also believed that semen is injected directly into the uterine cavity. Both Wernich<sup>14</sup> and Fehling<sup>4</sup> believed that the uterus contracts rhythmically during coitus and that a suction action is obtained by means of which sperm were aspirated into the uterine cavity. Sims<sup>12</sup> stated that the spermatozoa enter the cervix as it were suddenly; that the cervix is pressed forcibly against the glans by a contraction of the superior constrictor vaginae; that this pressure necessarily forces out the contents of the canal of the cervix; that the parts subsequently become relaxed, the uterus returns suddenly to its normal condition, and the seminal fluid filling the vagina is thus aspirated into the canal of the cervix. He stated that he had assumed the existence of a superior constrictor vaginae, with this function, but that he had made no dissection to prove the existence of such a muscle. Kehrer<sup>7</sup> supported an acute peristaltic action on part of the vagina. Litzmann<sup>8</sup> believed that during coitus the uterus descends and straightens out and that during a uterine contraction the cervix opens, and in this way semen is in part aspirated and also injected directly into the uterine cavity. Beck<sup>1</sup> suggested that the cervical lips dilate, the uterus descends and sucks semen into the uterine cavity, the cervix being endowed with erectile properties. Eichstedt<sup>2</sup> believed that the uterus assumes a globular form, a *cavum uteri* forms within it, and semen is aspirated into it through the open cervical canal. Kristeller<sup>6</sup> suggested that the cervical mucus plug is pushed into the posterior culdesac by the contraction of the uterus. The plug mixes intimately with the semen and the sperm adheres to it. Kristeller appears to have been the first to suggest that spermatozoa pass through the cervical canal by their own motility, in contradistinction to the previous writers who maintained that the female genital tract played an active part in the forward movement of the sperm. Strassman<sup>13</sup> and Seeligmann<sup>11</sup> postulate a possible chemotactic effect. The latter brought a drop of semen between a drop of vaginal secretion and a drop of cervical mucus and in a short time few sperm were found on the acid side, all dead, while on the other side there was an accumulation of living sperm. He considered this phenomenon to be a positive chemotaxis of the cervical mucus towards the sperm.

The materials used in our experiments were obtained from Vanderbilt Clinic and Sloane Hospital. The semen samples were collected by condom or directly into a sterile jar. In collecting the mucous samples, the external surface of the cervix was cleaned with a dry cotton ball. No lubricants or chemical solutions were allowed to come in contact with the cervix. A portion of the mucous plug in the lumen was then removed by aspiration with a clean sterile glass pipette. All samples were used as soon after collection as possible.

Microscopic observation of the phenomena occurring at the zone of contact between semen and cervical mucus is made as follows: A small fragment of cervical mucus, about 3 mm. in diameter, is removed and placed on a dry slide. A drop of semen of about the same size is placed on the slide about 3 mm. away from the mucus and a cover glass is dropped squarely on both. The cover glass should not be moved from

side to side. Under the weight of the cover glass both the mucus and semen will spread and their surfaces will come in contact without overlapping. A distinct phase boundary will result. The phenomena at this boundary are then observed under the microscope with a high dry power. If the cervical mucus is infected, very viscous, thick and opaque, the sperm in proximity to it will not accumulate at its boundary and will make no attempt to penetrate the mass. Occasionally a sperm or two will be seen a considerable distance within the mucus, due to faulty technic. There is no orientation of the sperm (Fig. 1).

If the same test is repeated with normal mucus, the picture is entirely different. The sperm in proximity to the mucus gather at the surface

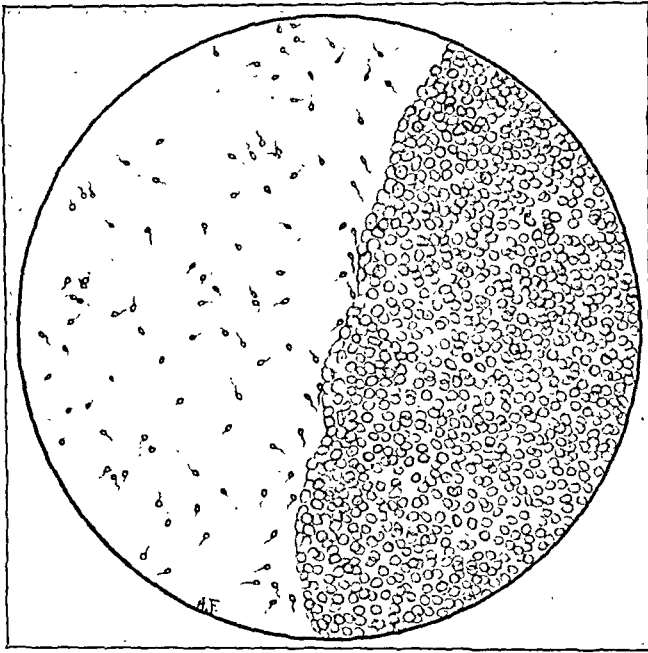


Fig. 1.—Contact between semen and infected mucus.

of the mucus, in rows two to four deep. All heads are pointed toward the mucus. The sperm have the ability to leave this zone, but unless they move a "considerable" distance away, they soon return to this oriented position. The sperm distant from the interphase move in their usual random fashion (Fig. 2). At many points sperm now begin to invade the mucus. The invasion is in the form of a somewhat triangular phalanx of oriented sperm, the apex of the triangle advancing first. The sides of the advancing triangle are composed of sperm oriented with their heads into the mucus and their tails in the excavated channel. The lashing of the tails produces a distinct current, and sperm may seem caught in it and swept backward. The advancing spear head of sperm may split and each column may now advance separately and in different direction (Fig. 3). With proper focusing and light a

halo of dissolved mucus may be seen about the sperm head. Some sperm after having advanced a certain distance lose their motility, but new, active sperm soon take their place. After a longer or shorter period the process ceases and the sperm lose their motility, perhaps because of the in vitro conditions of the experiment.

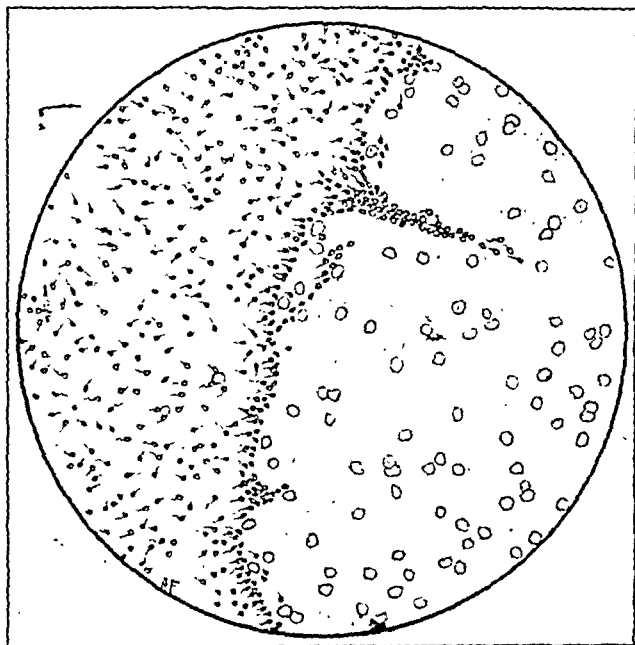


Fig. 2.—Contact between semen and normal mucus. Orientation and beginning penetration.

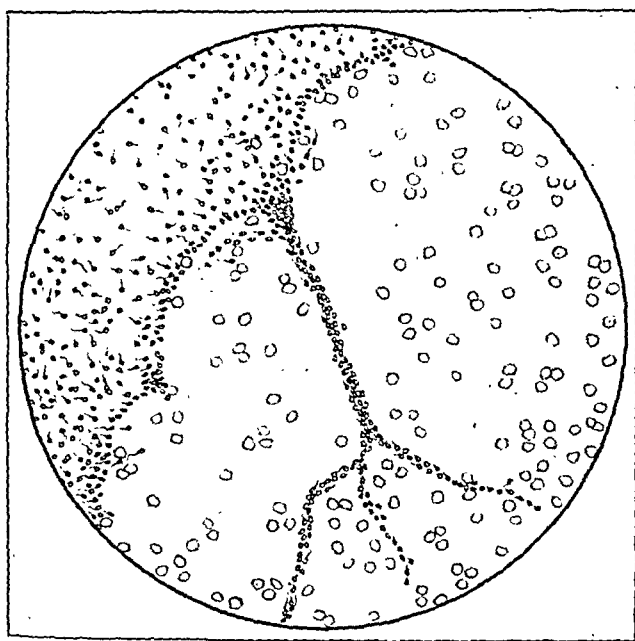


Fig. 3.—Contact between semen and normal mucus. Penetration more advanced than in Fig. 2.

We are now doing this semen-mucus phase boundary test in all cases of sterility. In some cases the absence of orientation and penetration on the part of the sperm is the only apparent cause for the sterile marriage. Not all specimens of sperm penetrate a given plug of mucus with equal facility. A given semen specimen, morphologically normal, may be unable to penetrate a given cervical plug, while a specimen from another male may do so quite easily. Infected cervical mucus is not penetrated at all, or only very slightly.

These observations confirm the belief that the sperm migration is related to the semen-mucus contact through some factor which acts as an orienting mechanism in the first stage of the sperm's journey in the tract. The actual penetration, and the ability of the sperm to advance in the viscous and adhesive mucus may well be related to the "mucolytic" enzyme previously described.<sup>7</sup>

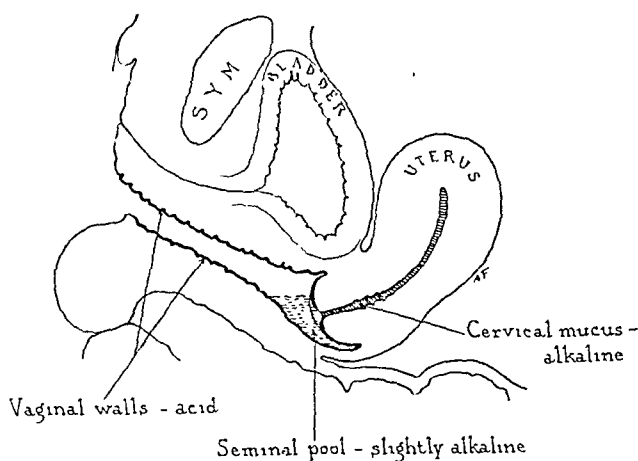


Fig. 4.—Diagram showing contacts between vaginal wall, semen, and mucus.

The normal acidity of the vaginal canal is about  $P_H$  3.5. This varies within small limits and is considered to be due to the conversion of the glycogen in the vaginal mucosa into lactic acid. The maintenance of the level of acidity probably has an important bearing on both the orientation and migration of sperm into and through the cervical mucus. In spite of extreme susceptibility toward acid, the sperm survive, in a seminal pool almost completely surrounded by an acid vagina, because the semen is a buffered solution, and addition of acid, up to certain limits, does not notably change the  $P_H$  of the semen. When the concentration of acid becomes high enough to overcome the buffer capacity of the semen, the motility of the sperm becomes markedly inhibited and soon ceases entirely. This usually occurs from two to six hours after coitus. To escape this destructive action of the lactic acid, it becomes essential for the sperm to move out of the seminal pool into the cervical mucus as soon as possible. Random swimming in the seminal pool would probably not be adequate for this.

The reaction of semen is very slightly alkaline, with a  $P_H$  of 7.8. If we consider the conditions which are present immediately after coitus, we find a seminal pool of slightly alkaline reaction, surrounded almost completely by an acid vagina ( $P_H$  3.5) and into this pool there dips a distinctly alkaline mucus plug ( $P_H$  9-9.6). We have therefore three layers of varying  $P_H$ , an acid layer (vaginal mucosa and secretion) in contact with a slightly alkaline semen, which in turn is in contact with a distinctly alkaline cervical mucus (Fig. 4). Such an arrangement gives two distinct phase boundaries: an acid (vagina)-semen interphase, and a semen-mucus interphase. At these interphases differences of electrical potential occur, with the  $P_H$  gradient as probably the most important factor. The  $H$  (and  $OH$ ) ions, having a much greater mobility than the other ions, diffuse more rapidly, thus causing a separation of charges and a potential difference across the boundary.

The possibility of this potential gradient being a factor in the orientation of the sperm migration was studied. To obtain data as to the probable magnitude of the gradient, semen and normal mucus plugs were brought in contact in a narrow tube; KCl-agar bridges connected either side of the couple with opposed calomel half-cells, which in turn were connected with a potentiometer-galvanometer set. The boundary potentials so measured were 3 to 5 millivolts (or, in a few cases, as high as 10), the mucus being electropositive to the semen. Assuming that the distance of the potential drop (the thickness of the phase boundary) was, at most, about  $50\mu$ , this gives a potential gradient of about 1 volt per cm. The initial value slowly fell to zero, as diffusion equilibrium was reached.

Experiments were done on the effect of a potential difference on the movement of normal sperm. The sperm carries a negative electric charge. If the two poles from a battery are placed in a suspension of sperm, and current allowed to flow, the cells move toward the positive electrode. This process, observed under a microscope, appears to be a cataphoresis, since there is no evident orientation of the direction of swimming (galvanotropism). Efforts to study this cataphoresis microscopically under very low voltage were unsatisfactory because of electric endosmosis, capillary flow, and especially because the active random swimming of the cells masked the cataphoretic movements.

A Pyrex glass U-tube was made of 6 mm. inside diameter, and 15 cm. total tube length, divided by two stopcocks (of 5 mm. bore) into three compartments. The middle compartment and the cocks were filled with seminal fluid, and the other compartments with Ringer solution buffered at  $P_H$  7.8. In the Ringer solution were put the tips of small agar-KCl bridges leading to Cu-satd.  $CuSO_4$  electrodes connected with a source of current as shown in the diagram (Fig. 5). The potential difference across the cell was calculated as:  $e = rI_1 - r'I_2$ , in which  $r$  is the

resistance across which the potential difference is developed by the battery current,  $r'$  is the resistance of the microammeter  $A_2$ ;  $I_1$  is the current in the battery circuit as indicated on the microammeter  $A_1$ ; and  $I_2$  is the current flowing in the cell circuit as read on the microammeter  $A_2$ . The variable resistance  $r$  was so adjusted, in our experiments, that the voltage gradient across the cell was from 10 to 50 millivolts per centimeter.

The stopcocks were carefully opened to prevent mixing of the fluids, and the switch closed. After one to four hours the stopcocks were carefully closed, the Ringer solutions removed from the tube and sep-

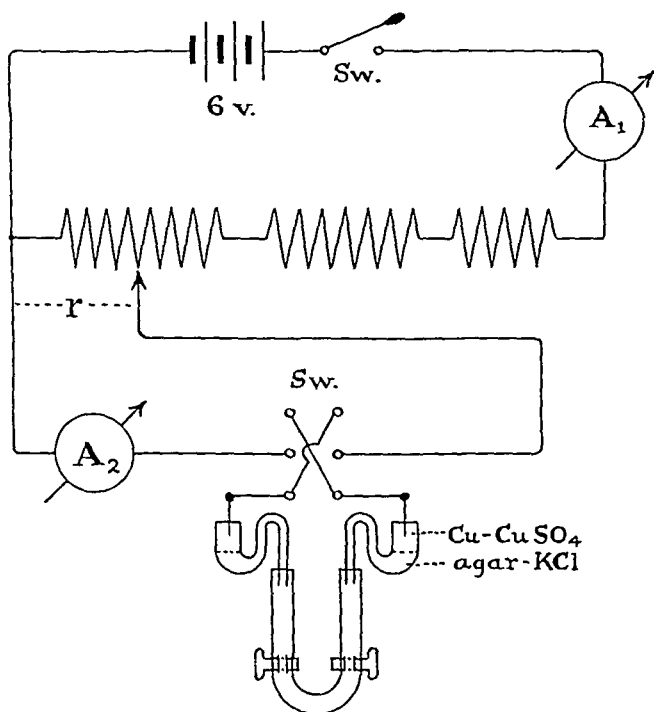


Fig. 5.—Apparatus for cataphoresis experiments.

arately centrifuged, and the sediment examined microscopically. The solution from the negative chamber invariably, in the whole series of experiments, was either sperm-free or yielded at most one to three sperm in the whole of the material when thoroughly searched with the microscope. The positive chamber, however, in every case showed an average of from three to eight sperm in each high-power field.

These experimental results indicate that one factor in the initial orientation of the sperm migration is a difference of electric potential causing a cataphoretic effect, thus suggesting a mechanism that may be the basis of the "chemotaxis" observed. Abramson<sup>15</sup> has somewhat similarly postulated a potential gradient as a factor in the migration of leucocytes in inflammatory processes in tissues.

It has already been remarked that when the cervical mucus plug becomes infected, it no longer shows the penetration phenomenon with semen as described above; nor is it "digestible" by the lytic enzyme present in normal semen.<sup>7</sup> When such a mucus sample is tested with semen by the boundary potential method, one finds that the potential difference is reduced almost to zero, or even actually reversed in polarity. The reaction of the infected mucus is less alkaline than the normal, or it is even frequently distinctly acid, so that the  $P_H$  gradient with its diffusion potential disappears. Such changes would, we believe, greatly hinder the normal mechanism of sperm orientation and migration.

#### SUMMARY AND CONCLUSIONS

A technic has been described for observing the phenomena occurring at the contact between semen and cervical mucus, and the appearance of the mucus-penetration by the sperm has been discussed. The method has been of use in clinical work.

The contact zones between vagina ( $P_H$  3.5) and semen ( $P_H$  7.8), and between semen and cervical mucus ( $P_H$  9-9.6) present a gradient in electric potential across the boundaries. The boundary potential between semen and mucus has been measured in vitro, and found to be of the order of 3 to 5 millivolts. This potential difference has been shown to be adequate to cause cataphoresis of the sperm cells, and it is suggested that it is a factor in the first orientation of sperm migration in the tract.

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## INTRACRANIAL BIRTH INJURIES

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**I**N REVIEWING recent statistics concerning the incidence of birth trauma, we find a marked increase in intracranial lesions, and it would seem wise that as obstetricians we review our methods of conducting labor, with especial consideration of the forces which are exerted upon the fetal skull and its contents during its passage through the birth canal, in order to reduce the present alarming number of injuries and deaths.

The subject may be approached from several different angles. First, it is essential to review the anatomy of the fetal head and its membranous supports. Secondly, we must know something of the cranial mechanics involved in the passage of the head through the pelvis of the mother. Thirdly, we must consider the effects of labor upon normal and abnormal positions of the fetal head and its supports. Fourthly, we must discuss measures to prevent intracranial hemorrhage. Treatment of the newborn child and the signs of hemorrhage after birth will not be included in this discussion.

### ANATOMICAL REVIEW

The fetal cranium is composed of a vault, constructed of thin plates of elastic cartilage, loosely bound together with fibrous tissue, and anchored to a rigid, noncompressible base. These plates of soft bone are easily compressible from all sides, are fractured by comparatively slight force and may be caused to override if unequal pressure is exerted upon them. They are attached to the base by fibrous tissue which allows them to move back and forth. This is particularly marked in the occipital bone, the movement of which is backward and forward, thus increasing or decreasing the anteroposterior diameter of the head. This change in position of the bone determines the degree of molding which the head may undergo during labor.

The cranial bones are protected exteriorly by the skin, subcuticular tissue, muscles and fascia; interiorly, they are held together by fibrous tissue and the dura mater, the outer edge of the dura forming the periosteal covering. They are also held in place by the contents of the cavity, and by the pressure exerted intracranially by the cerebrospinal fluid. The dural septa play an important part in protecting the fetal brain from damage due to distortion or excessive molding of the bones; these septa are of the same structure as the dura, and extend into the intracranial cavity, dividing it into three chambers. The horizontal septum, or tentorium cerebelli, is formed at the lateral sinus, and divides the intracranium into two chambers, the supratentorial cavity and the subtentorial cavity. The supratentorial cavity, which is divided vertically by the second dural septum or falx cerebri, is occupied by the hemispheres of the cerebrum; the subtentorial cavity, divided vertically by a third dural septum, the falx cerebelli, is occupied by the cerebellum, the medulla, and the pons.

The dura which lines the cranial cavity is continuous with the spinal dura, and is composed of an outer endosteal layer and an inner meningeal layer.



The inner layer is smooth and moist, and is in direct contact with the brain and spinal cord. The dura is adherent to the skull bones, the edges of the foramen magnum, the posterior longitudinal ligament, the second and third cervical vertebrae and the sacrum. The dura of the skull and spinal canal forms a membranous container, its contents being the brain and spinal cord, surrounded by a watery fluid contained in the subarachnoid space and called the cerebrospinal fluid. This fluid is under tension, which is equalized between the head and the spinal canal at the foramen magnum, where the subarachnoid enlarges to form the cisterna magna. This tension tends to keep the brain and spinal cord in place, not allowing them to be pressed upon by the surrounding bones. It plays an important part in labor, preventing the medulla, the vital center, from



Fig. 1.—The vertical system, indicated by Arrow 1, passes through the structure of the falx cerebri and the tentorium cerebelli. The former originates at the Crista Galli anteriorly, passing backward in sickle-like fashion to insert into the tentorium cerebelli at the juncture of its two lateral halves. It is definitely constructed to withstand pressure. It consists of two opposing sets of converging fibers, one set arising chiefly from the middle two-thirds of the falx cerebri and the other beginning in the tentorium. These converge, forming a heavy point of union called the white line. Arrow 2 indicates fenestra of the falx cerebri. These are normal openings, although they are not found until the seventh month of intrauterine life. Until that time the falx is thicker at this point.

being crowded into the foramen magnum by too severe pressure upon the head. It is with the dural septa and the cerebrospinal fluid that we are particularly concerned in considering the mechanics of the cranium.

Besides carrying the blood vessels, the dural septa are designed to resist cranial distortion and control intracranial pressure, as they are composed of folds of the meningeal layer of dura strengthened by bands of white elastic fibrous tissue arranged on a definitely mechanical principle. These bands are of particular interest during labor. Holland stated, in 1924, that they "should be regarded as stays to the cranial bones"; and he has divided them into two systems, the vertical and the anteroposterior. These two systems are shown in Figs. 1 and 2.

These bands are of tough structure, but are slightly elastic. They can be

found beginning to develop as early as the fifth month of intrauterine life. This elasticity together with the mobility of the cranial bones, makes possible the condition known as molding, which is found during labor in all cases, to a greater or less degree. Change in size or shape of the fetal head is a beneficial thing, up to a certain point, as it helps to accommodate the vertex to the birth canal. It occurs at the beginning and during the first and second stages of labor. Until this time there is very little opportunity for molding to occur, except possibly during the last month of pregnancy, when the head is lowered into the pelvis by mild uterine contractions and the thinning of the lower uterine segment and beginning effacement of the cervix. Before this time there is very little change in the tension of the dural septa, but as soon

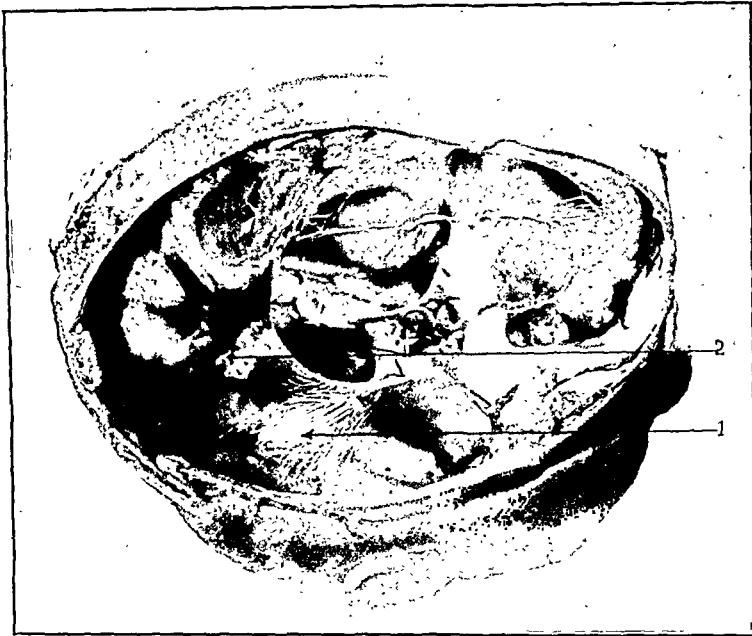


Fig. 2.—The anteroposterior system, indicated by Arrow 1, passes through the structure of the tentorium, which arises laterally at the margin of the sphenoid and occipital bones, and passes horizontally inward to unite with the falx cerebri and the falx cerebelli. It also passes anteriorly in a fanlike formation to insert into the anterior clinoid processes. The falx cerebelli, not shown in the cut, originates in the foramen magnum, and passes vertically to insert on the under surface of the tentorium and falx cerebri, helping to form the white line. The white line, indicated by Arrow 2, a heavy fibrous band, passes posteriorly to insert into the occipital bone opposite the torcular sinus and occipital protuberance. Anteriorly the white line divides to form the incisura through which passes the midbrain.

as the head begins to mold, a positive tension is exerted upon these fibers. If the molding is unequal or excessive, it causes actual cranial distortion. Whether or not this occurs depends upon the pressure exerted upon the head, its position, and the degree of resistance it meets from the surrounding structures. If the pressure is equal from all sides, very little change of shape can take place. This is usually the case in normal deliveries where there is no outside pressure other than that exerted by the soft parts. Increased pressure through one or the other of the diameters of the head causes molding.

Excessive molding or cranial distortion is seen most frequently in cases where the head presents itself abnormally, such cases as occipitoposterior, face, brow, or breech presentation, or in contracted pelvis with disproportion between the head and the pelvis. The majority of deaths and deformities result from these abnormal positions and conditions.

## OCCIPITOPOSTERIOR POSITION

The frequency of the occipitoposterior position has been underestimated in the textbooks and today it is seen more often than ever before. The fetal mortality is rather high, and fetal accidents occur in a large percentage of the cases. Molding is very marked and the head becomes elongated.

Quite frequently the membranes rupture early and labor begins slowly, the head entering the pelvis either on the left or the right oblique, depending upon whether it is a left or right position. Often the base of the skull does not become engaged or pass through the



Fig. 3.

inlet until late in the first stage or early in the second, and only the loosely connected vault receives the pressure of labor. In the occipitoposterior position pressure is exerted along the anteroposterior diameter. The occipital bone, as a result of its hinge-like action and its relationship to the maternal sacrum, moves forward under the parietals. The frontals likewise move posteriorly under the parietals, which move inward, due to outside pressure and a similar type of attachment to the base. The result is that the anteroposterior diameter is decreased, and the vertical diameter is correspondingly increased. This has a definite effect upon the dural septa and their enforcing bands. This effect can best be shown by placing a dissected fetal head with membranes in a posterior position in a pelvis cut sagittally and observing the result. This may be seen in Fig 3.

We find that the middle two-thirds of the falx cerebri, shown by Arrow 1 (Fig. 3), containing one set of the vertical fibers, tightens,

together with the tentorium, which is also elevated. The free edge of the falx cerebri relaxes, as shown by Arrow 2. The reason for the elevation and tightening of the tentorium is that these vertical fibers are attached both to the skull and to the white line and tentorium, and as the cranial bones turn inward from anteroposterior and transverse outside pressure, the vault is elevated, pulling the fibers and the tentorium upward with it. If the head is allowed to be jammed into the pelvis without relief from this pressure, molding is excessive and the head becomes distorted. This causes the characteristic "feel" that we often notice, on vaginal examination, with this position, the head



Fig. 4.

seeming to have become pointed. If this distortion continues long enough, the dural septa give way, with laceration of the vertical fibers, and occasionally of both sets. This is shown in Fig. 4, as indicated by Arrow 1. This patient, a multipara, had a twelve-hour, severe, dry labor; R. O. P. mechanism; medium forceps used after manual rotation, resulting in a stillbirth. Very little analgesia was given during the first stage, during which time the fetal heart was unsteady.

Laceration of the fibers is followed by a change in the balance of the intracranial pressure, and hemorrhage results from rupture of the tributaries of the veins about the incisura. Or if, after rupture of the

septa, hemorrhage does not take place, but the delivery becomes difficult, forceps perhaps being required, the intracranial balance is no longer present within the skull, as shown by the looseness of the cranial bones, which overlap one another, tearing the underlying sinuses, or crowding the medulla into the foramen magnum with death due to pressure, edema, or hemorrhage. It is wise in labors complicated by the posterior position and early rupture of the membranes to watch the first stage of labor very closely, relieving pressure upon the head rather frequently. These labors are apt to be long and tedious, and plenty of relaxing drugs should be given, as morphine, chloral hydrate, bromides, or ether in oil without the quinine. If overpressure upon the head is apparent before delivery can be executed, as shown by irregularity in the fetal heart rate, it may be good judgment to insert a Voorhees bag, not too tightly inflated, to relieve the cerebral pressure. However, before doing this it is necessary to rule out heart irregularities due to cord pressure. The patient should not be encouraged to voluntarily aid herself in expelling the child by bearing down; this does not hasten the delivery. It may become necessary to change the position of the vertex to an anterior one, when the cervix becomes sufficiently dilated for the hand to be inserted without injury to the cervix. After rotation, the head should be allowed to pass through the pelvis spontaneously, allowing time for the intracranial pressure to adjust itself and for molding to take place. High forceps and version are dangerous in this type of case; spontaneous delivery will give the fetus a better chance unless the second stage becomes too prolonged. Failure to make a definite diagnosis of this position may result in a very prolonged second stage. This stage is particularly dangerous to the fetus because of the increasing extension of the head which usually occurs, and the depression of the frontal bones caused by symphysis pressure. With this condition compensatory increase in the vertical diameter of the head is limited; molding can no longer go on, and the cranial bones begin to overlap, causing damage underneath. In all cases of this position, frequent recording of the fetal heart is necessary.

#### FACE AND BROW PRESENTATION

In face and brow presentation a similar story can be told, and the mortality has been estimated as high as 15 per cent. However, the mechanics causing septal tears differ from those of the occipitoposterior position. In face and brow presentation the largest diameter of the head attempts to pass through the pelvis, and severe pressure is exerted over the bregma or over the vault and base. In this type of pressure, the occipital bone passes backward, the frontals are depressed, the anteroposterior diameter is increased, and the vertical is correspondingly decreased.

Where the presentation is of this type, as shown in Fig. 5, the free

edge of the falx cerebri and the tentorium become tense, as indicated by Arrow 1, but the remaining portion of the falx becomes loose and slack, owing to the approximation of its attached end and its free margin by lowered elevation of the vault of the cranium, as shown by Arrow 2. Rupture of the free edge occurs, together with laceration of the anteroposterior set of fibers, as shown in Fig. 6, indicated by Arrow 1. This shows a dissected fetal head. The mother was a multipara. She had a long dry labor, followed by a forceps delivery resulting in stillbirth. Cases with this presentation are characterized by long and difficult labor, the result being the changes in the head described above. If it is apparent that this position cannot be delivered spontaneously, it is better to correct it early if this can be done with



Fig. 5.

safety. Otherwise spontaneous delivery is desirable, as the added bilateral squeezing of the head by pressure of the forceps may increase the possibility of intracranial damage. A head allowed to remain in this position too long will so mold that after correction it is almost impossible to bring the vertex through the pelvis. This changes the point of pressure from one set of fibers to another and allows them to be unduly stretched. When the chin is posterior, delivery is impossible unless the pelvis is large and the child small. The pressure upon the bregma is severe, and complete tears of the septa are very frequently found, which accounts for the extremely high fetal mortality. Conversion of this position is absolutely essential before delivery can be completed, and it should be done as early as possible. In this type of labor, as in the foregoing, it is necessary to ease the patient by the

use of relaxing drugs. The obstetrician should also be thoroughly familiar with the construction of the pelvis, as contractions, tumors, etc., may cause these abnormal positions.

#### BREECH PRESENTATION

Various observers have noted that rupture of the dural septa occurs frequently in breech presentation, some estimating the percentage as high as 90. Statistics show a high fetal mortality and deformity each year as a result of this abnormal presentation. In this condition there is abnormal physiologic molding, there having been no time for slow molding or adjustment of the fluid pressure to occur, the head entering the brim within a few seconds. If it fits it tightly, and delivery is



Fig. 6.

somewhat retarded, the operator or his assistant exerts pressure over the vertex. This pressure is often severe, sudden, and caused by the hand rather than the uterus. In spontaneous breech delivery, when no pressure from above is necessary, the vertical diameter of the head is increased by the turning in of the bones from outside pressure, particularly the occipital bone. When pressure upon the vertex from above is necessary, this compensatory increase in vertical diameter cannot take place, but instead there is an actual increase in the anteroposterior diameter. This results in laceration of the free edge of the falx cerebri or tentorium near the junction of the vertical and anteroposterior sets of fibers. This is shown in Fig. 7, and indicated by Arrow 1. This laceration causes a descent of the tentorium, a lowered level of equalization of pressure, a decrease in the amount of fluid in the subtentorial cavity above the foramen magnum, and consequently a possible herni-

ation of the medulla into the foramen magnum with death of the fetus from pressure upon the vital centers. At the same time there is absence of pressure along the vertebral column toward the head; instead, rather severe traction is exerted upon the trunk, causing an elongation of the spinal canal and spinal dura. As the spinal dura is attached to the foramen magnum, second and third cervical vertebrae, and sacrum and, as it is surrounded in the epidural space by a material that is gelatinous and noncompressible in character, its lumen is not reduced. Owing to its elasticity, its length is increased, more fluid being sucked into the spinal canal, aided by pressure upon the head. Beneke found in 1910 that the spinal column and cord could be stretched two inches without tearing. But if too severe traction be exerted upon the trunk, complete

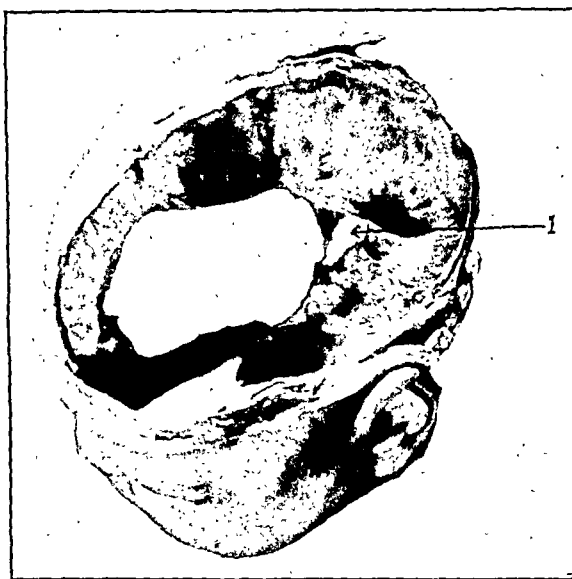


Fig. 7.

rupture of the spinal cord may result, or rupture of the first cervical vertebra and the dural septa.

It has been a long standing belief that only eight minutes should be allowed for delivery of the head and shoulders after the umbilicus has passed the vulva. Consequently hurried extractions have been done, with damage to the fetal head, brain, and spinal cord. Pike and Gomez, in a series of experiments, found that the nerve cells of the cortex could stand total anoxemia for ten minutes, while those of the medulla could live without oxygen for twenty minutes. If we assume this to be true, fifteen to twenty minutes may be allowed for delivery of the head and shoulders without dangers to the fetus.

During a breech extraction the body of the fetus must be directed through the proper plane of the pelvis. In order to do this it is necessary to have the buttocks of the mother overhang the edge of the table or bed; otherwise angulations occur which necessitate more pull



upon the trunk. The head should be delivered through the diameter which it best fits. The vertex should be flexed, before attempting entrance into the pelvis, by pressure upon the occiput externally and over the alveolar margin of the maxilla internally; this tends to bring the smallest diameter through the pelvis. It is also true that a flexed head causes a better distribution of pressure along the dural septa and thus a more constant intracranial pressure. The use of forceps upon the aftercoming head is a wiser measure than too severe abdominal pressure by an assistant upon the vertex. The forceps designed by Piper are of particular advantage for this maneuver. They control intracranial balance better and pressure is exerted more uniformly over the vertex.

#### CONTRACTED PELVIS

Contracted pelves are responsible for a large number of fetal deaths and accidents. Where the pelvis is markedly decreased in size, as in the so-called absolute contraction, there are probably fewer instances of such disaster; it is with the border-line cases that we find the greatest difficulty, and in them we have our high fetal mortality.

In contracted pelvis there exists a disproportion between the size of the fetal head and of the pelvis, so that only the vault enters the brim and is pressed upon by the bony structures. It is the promontory of the sacrum which does the most damage, as it juts forward. In these cases we do not have molding but overlapping of the cranial bones, which may be felt by vaginal examination, and the resulting cranial distortion is severe. The dura may be actually torn away from the bones, causing tears of the blood sinuses and extravasation of blood intracranially. With this distortion the dural septa are stretched unequally, and laceration of them frequently occurs, often involving the entire group. There is no chance for a compensatory increase in any one diameter of the head to occur as a result of unequal pressure.

It is my opinion that careful measurements of the pelvis, together with a test of engagement of the head during the last month (the so-called Mueller test), and careful management of the early part of the first stage of labor as regards asepsis and progress, should eliminate some of the difficulties of delivery in cases of contracted pelvis.

#### FORCEPS

In any case of fetal death from intracranial hemorrhage the question is always raised as to whether forceps were used. It is hardly likely, however, that such fatalities can result from the proper use of forceps. Where forceps are used without regard to the relative position of the head and pelvis, fetal deaths and deformities are more prone to occur. If forceps are used, care must be taken to apply them in front of the ears, where the base of the skull can act as a wedge between the blades and avoid bilateral squeezing of the vault, which results in an increase

in the vertical diameter of the head. Also, if forceps are applied to the largest diameter of the head they will cause pressure, because the average occipitofrontal diameter measures  $11\frac{3}{4}$  cm., while the transverse width of the blades is only 8 cm.

In using either high, medium or low forceps, it is essential to bring the head through the diameter of the pelvis which it will best fit. Care should be taken not to extract too quickly, but to allow time for molding to occur. Traction should be made synchronously with the uterine contractions, as the intracranial pressure is then more uniform, due to the pressure of the uterus along the vertebral column toward the head.

Allowing a fetal head to rest upon the perineum for hours without relief may have as serious results as too rapid extraction. A prolonged second stage of labor has serious effects upon the fetal head. The "low prophylactic forceps" of DeLee and the "forceps control" of Pomeroy probably have done much to reduce the incidence of cerebral hemorrhage. The use of forceps in this manner tends to protect the dural septa from outside pressure, the forceps taking some of the force. We know that when the vertex has reached the vulva the external pressure upon it is released, while the pressure upon the trunk is increased, so that there is an increase in the amount of blood within the head. Forceps tend to hold this intracranial pressure more uniform, preventing a sudden increase of blood in the cerebral structures. I feel that many babies are lost at the outlet; they have survived the strenuous first stage of labor and part of the second, but when they reach the outlet another mechanism comes into action. If the head comes through in flexion, as it usually does, as soon as the outlet is reached extension begins, shifting the point of pressure from one point on the dural septa to another. The reverse takes place if the head comes through the pelvis in extension. In other words, first one set of dural fibers is used and then the other. In a rapid, spontaneous delivery this change is very marked, and should be guarded against.

#### UTERINE STIMULATION AND INDUCTION OF PREMATURE LABOR

As the time for labor approaches, the uterus prepares itself for the ordeal of expulsion of the child. The lower segment softens, retracts, and becomes ready for dilatation of the cervix. The body of the uterus begins to contract, at first mildly and infrequently, giving the fetal head a chance to slowly adjust itself to the newly exerted pressure. As labor goes on, more and more pressure is exerted by the uterine contractions above and by the counter pressure of the soft and bony parts of the mother below. It is difficult to say what is the safest method of labor induction as regards cerebral damage, for occasionally after induction, labor sets in so rapidly that expulsion soon takes place, and this sudden onset (particularly after rupture of the membranes), with frequent and tumultuous pains and very rapid dilatation of the cervix,

may result in death of the child. This is usually foreshadowed by the presence of meconium in the amniotic fluid, and by a slowing of the fetal heart, indicating cerebral pressure. This condition is seen particularly in cases where uterine stimulation has been severe, or where pituitrin, quinine, or ergot has been administered. The fetal head undergoes such rapid changes in the distribution of pressure that it does not have time to adjust itself to the new situation. There is little chance for stretching of the dural fibers to take place, and instead rupture may occur.

Where labor occurs or is induced prematurely, fetal death may occasionally result from similar causes. The premature child presents a poor development of tissue. Labor in such cases is usually rapid, the elastic bands of dural septa are fewer in number, and as a result severe dural ruptures are frequently found. Such a condition is shown in



Fig. 8.

Fig. 8. These membranes were removed from a seven months' stillborn child; in this case labor was induced on account of diabetes mellitus, and delivery was rapid and spontaneous. At autopsy, comparatively few elastic fibers were seen, and a complete laceration of both sets of fibers was found. I personally have observed fewer septal tears and fewer fetal deaths in premature babies that have been delivered breech; in this mechanism there is apparently less cerebral pressure, as the fetal body has prepared the soft tissues and there is little bony obstruction to the aftercoming head.

#### SUMMARY AND CONCLUSIONS

Upon the integrity of the fetal head and its contents depends the future of the child. Labor should not be considered from the maternal standpoint alone, but some thought should be given to the mechanics of the fetal cranium and its supports. We teach our students the mechanism of labor, but we rarely devote much time to instruction regarding the mechanics of the fetal skull. But when a patient consults

an obstetrician, she demands not only her own recovery and a living child, but also an offspring she will be proud to own as it grows toward manhood or womanhood. This can only be assured by careful prenatal care, a proper understanding of the mechanism of labor and of the fetal skull, correct diagnosis of the position of the child and its relationship to the pelvis, and careful observation during the progress of labor.

In conclusion I wish to stress the following points:

1. The fetal brain is protected against the forces of labor by several mechanisms, of which the dural septa and the cerebrospinal fluid are perhaps the most important.
2. The balance of intracranial pressure is controlled by these membranes and the cerebrospinal fluid.
3. Laceration of these membranes allows a disturbance in the intracranial pressure balance, which in turn causes distention and rupture of the blood vessels and sinuses.
4. The dural septa are torn in cases of abnormal position with disproportion, in faulty application of forceps, in rapid normal and premature labors, and in hurried breech extraction.
5. More carefully watched first and second stages of labor will reduce the incidence of intracranial injury.
6. Greater conservatism in the induction of premature labor and in the use of mechanical procedures will reduce the number of fetal accidents and deaths.
7. Finally, a better understanding of the mechanism of labor, and also of the mechanics of the fetal skull and its supports will tend to lessen the incidence of such occurrences.

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601 MEDICAL ARTS BUILDING.



## TRANSVERSE PRESENTATION

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WHILE transverse presentation of the fetus is a well known cause of dystocia, analytical studies of this abnormality based on extended series of cases are apparently few in number. The monograph of Zangemeister,<sup>1</sup> published in 1908, was concerned only with neglected cases. Similarly, the reports of Herrgott,<sup>2</sup> of Stephenson,<sup>3</sup> and of Franz,<sup>4</sup> dealt chiefly with special aspects of this condition such as spontaneous evolution and birth by *conduplicato corpore*. Again, a long series of studies have issued from German clinics devoted to the optimum time for performing version in transverse presentation. These date back some forty-five years to a period when it was a common practice to effect combined podalic version in all cases of transverse presentation which permitted the introduction of two or more fingers through the cervix, the procedure being followed, of course, by an interval of waiting until complete cervical dilatation allowed extraction. In 1886, Winter<sup>5</sup> opposed this practice by showing that internal podalic version, unless followed by immediate delivery, resulted in a high fetal mortality and accordingly he counselled deferring version until the os was completely dilated. Apparently the views of Winter have been accepted by about half the obstetricians of Germany, with the result that an active polemic has ensued in that country and an abundant literature developed. While most of these papers are obviously controversial in nature and are limited to the one subject under discussion, a few of them, particularly that of Sachs and Poecke,<sup>6</sup> are comprehensive analyses of large series of cases.

The present paper comprises a study of the 147 cases of transverse presentation which have occurred in the Obstetrical Department of the Johns Hopkins Hospital since its opening in August, 1896 until April, 1931. Cases of transverse presentation in which the position changed to vertex during labor (whether spontaneously or as the result of external version) have been omitted from consideration, since it was difficult in many of them to be certain that we were dealing with bona fide examples of this abnormality. Likewise, cases of transverse presentation in twin pregnancies have been omitted from the series. It is the object of our study to analyze those factors which most frequently cause

dystocia in this condition and, more particularly, to single out the various complications responsible for the high fetal mortality associated with it. Well established facts concerning transverse presentation, such as incidence and etiology, will be touched upon but briefly and then only in so far as they are of practical import.

#### ETIOLOGY

Our 147 cases of transverse presentation fall into three main classes, one a group of 93 cases in which the fetus weighed 2500 gm. or more, another comprising 38 cases in which the fetus weighed between 1500 and 2500 gm., and thirdly, a group of 16 cases, classified as abortions,

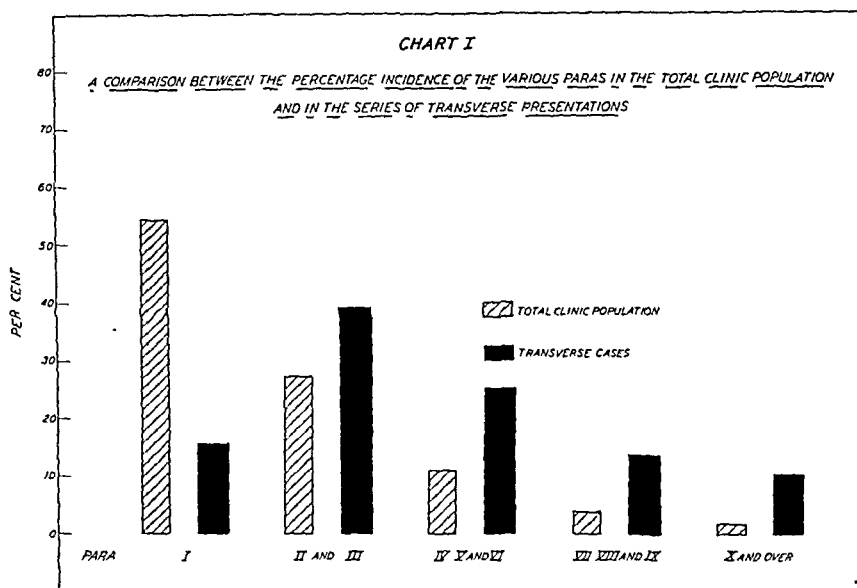


Chart 1.—Showing the increasing incidence of transverse presentation with advancing multiparity. For example, the first column on the left (striated) shows that primiparae comprised 54.6 per cent of our total Clinic population, while the second column (black) shows that, in the group of transverse presentations, primiparae made up but 15.4 per cent. The chart is based on 17,858 consecutive full-term deliveries in the Clinic including 93 full-term cases of transverse presentation.

the fetus weighing under 1500 gm. The presumable cause of the abnormality, in the 93 cases in which the fetus was mature, was as follows: contracted pelvis, 38 cases; multiparity, 33 cases; excessive size of the fetus, 8 cases; cause unknown, 7 cases; previous uterine suspension, 6 cases; placenta previa, 5 cases; pelvic neoplasms, 2 cases; and justo-major pelvis, 1 case. The rôle of multiparity in predisposing to transverse presentation was particularly striking in this series and is shown diagrammatically in Chart I. It will be noted that approximately one-half of the patients with transverse presentations had had three or more previous babies, whereas in the Clinic as a whole, only 17.8 per cent of the patients had borne that many children. Considering the mothers who had had nine or more previous deliveries, it will be seen that patients

of that parity made up only 2.4 per cent of the total number of women delivered in the Clinic, but they constituted about 10 per cent of the cases of transverse presentation. Previous uterine suspension has been listed as a cause of transverse presentation on the ground that the occurrence of 6 such cases in the 93 seems more than a coincidence. It would appear conceivable, moreover, that suspension operations might, in isolated cases, produce sufficient distortion of the uterine axis to prevent proper engagement of the head and thus be responsible for occasional instances of this abnormality.

In the 38 cases in which the baby was premature, contraction of the pelvis played a less important causative rôle. The presumable causes of the transverse presentation in this group were as follows: multiparity, 14 cases; placenta previa, 8 cases; cause unknown, 8 cases; contracted pelvis, 6 cases; and introduction of a uterine bag, 2 cases.

#### MATERNAL MORTALITY

In the series of 147 cases there were 4 maternal deaths, an incidence of 2.7 per cent. An additional patient (Case 1), left the hospital against advice on the 7th day postpartum and died at home 6 days later. Brief histories of these five fatal cases follow.

CASE 1.—(Unit No. 12,836) The patient was a thirty-six-year-old colored multipara, para ix, who had not been registered on the service. Her membranes ruptured with the onset of pains and after one hundred and twenty hours of labor at home, where repeated vaginal examinations had been made by a midwife, she was admitted to the hospital with a temperature of 104.4° and a pulse of 140. Examination showed that the uterus was tetanically contracted around a small child in transverse presentation; the fetal heart sounds were not heard. The cervix was 5 cm. dilated with placental tissue extending half over the partially dilated cervix. The delivery, which was rendered difficult by the presence of a Bandl's ring, was effected by embryotomy, the fetus weighing 1136 gm. During the first week of the puerperium, hectic elevations of temperature, reaching 104.4°, occurred daily. On the seventh day postpartum, the patient left the hospital against advice and died at home on the thirteenth day following delivery.

CASE 2.—(Unit No. 18,924) The patient was a twenty-eight-year-old colored multipara, who had not been registered on the service. Her membranes ruptured prematurely, labor ensuing in about twelve hours. After twenty hours of labor at home, where one or more vaginal examinations were made by a private physician, she was admitted to the hospital with a temperature of 103.8° and a pulse ranging between 150 and 160. Examination showed that the uterus was tetanically contracted around a small child in transverse presentation; the fetal heart sounds were not heard. The cervix was 3 cm. dilated. The patient was delivered by removal of the unopened uterus, which contained a 2000 gm. stillborn fetus. The patient died immediately after the operation.

CASE 3.—(Hist. No. 12,058) The patient was a thirty-nine-year-old white multipara, who had not been registered on the service. She was admitted to the hospital after nine hours of labor at home, the membranes having ruptured eleven hours before the onset of pains. There was no history of vaginal examinations having been made outside of the hospital. Upon examination it was found that the blood

pressure was 210/130 and that the urine contained 4 gm. of albumin per liter. A small fetus lay in transverse presentation with its heart sounds audible. The cervix was 6 cm. dilated. The patient was delivered by manual dilatation, version, and extraction, of a living child, weighing 2030 gm. There was considerable postpartum hemorrhage, the measured blood loss being 1200 c.c.; bilateral cervical lacerations were found, and these were supposedly repaired. Throughout the delivery the patient's pulse was of poor quality and three hours afterward, despite the usual stimulating measures, it became weaker and more rapid; she died nine hours postpartum, the clinical picture being that of shock. Autopsy revealed that the cervical tears had been incompletely repaired and extended up into the uterine wall 9 cm. above the highest suture. However, there was no intraperitoneal hemorrhage. The kidneys were small with the cortex thinned to 2 mm.; the glomeruli showed old scarring with increase in fibrous tissue between the tubules. The liver showed focal necroses and the heart old mitral endocarditis.

CASE 4.—(Hist. No. 5386) The patient was a twenty-five-year-old colored multipara, para iv, who had been registered on the service; she had a borderline contraction of the pelvis, the diagonal conjugate measuring 11.5 cm. As soon as she was definitely in labor, she entered the hospital, no examinations having been made at home. It was found that a small child lay in transverse presentation; the heart sounds were not audible; the membranes were intact. After ten hours of labor, the membranes ruptured at complete cervical dilatation and a 2010 gm., stillborn fetus was delivered by spontaneous evolution. Although the first seven days of the puerperium were afebrile, on the eighth day hectic elevations of temperature began and the patient died on the seventeenth day postpartum. Autopsy showed puerperal infection with acute endometritis; infected thrombosis of the sinusoids of the uterine wall; extension of the thrombus into the uterine veins; fibropurulent peritonitis and general septicemia.

CASE 5.—(Unit No. 30,193) The patient was a thirty-two-year-old colored multipara, para v, who had been registered on the service. During the eighth month of pregnancy, while at home, she had a painless hemorrhage which was estimated at about 500 c.c. She was brought immediately to the hospital, where examination revealed a small child in transverse presentation; the fetal heart sounds were not audible. The cervix, which was 4 cm. dilated, was covered entirely with placental tissue. Plans were made to insert an intraovular bag, but when the placenta was perforated for this purpose, a foot was immediately palpated, and it was thought preferable to effect a Braxton-Hicks version. This was done and gentle traction exerted by means of a strip of gauze tied to the foot. The small child, which weighed 1370 gm., was gradually extracted, the procedure being facilitated by craniotomy on the aftercoming head. Since moderate bleeding followed the removal of the placenta, the uterus was packed; no cervical lacerations were visible. The patient was returned to the ward in good condition, but three hours later, her pulse became rapid and thready and her respirations shallow and accelerated. There was negligible external hemorrhage, but despite the usual stimulating measures the patient died four hours postpartum, with the clinical picture of shock. Autopsy showed rupture of the uterus with hemorrhage into the left broad ligament.

It should be noted that all of the five deaths occurred in immature or premature labors, the largest child weighing 2030 gm. In two of our five fatal cases, placenta previa was an important, if not the determining factor in the death of the patient. In three of them the dystocia was essentially cervical in character. Thus, in Case 1, the cervix was found to be 5 cm. dilated after one hundred twenty hours of labor; in Case 2, it



had reached a dilatation of only 3 cm. after twenty hours; while in Case 3, it had become 6 cm. dilated following nine hours of labor, but tore to a fatal degree during the delivery. Recalling that all of these patients were multiparae and that the weights of the babies were 1136, 2000, and 2030 gm. respectively, it seems altogether probable that the outcome in these cases would have been more favorable had it not been for the slow and incomplete dilatation of the cervix. We believe, in fact, that the danger to the mother in transverse presentations rests not so much in the mechanical difficulties associated with the transverse lie of the fetus per se, but rather in certain accompanying conditions, particularly early rupture of the membranes, incomplete dilatation of the cervix and placenta previa, complications which are often the precursors of intrapartum infection and rupture of the uterus.

#### FETAL MORTALITY

The fetal mortality in the 93 cases in which the fetus weighed over 2500 gm. is shown in detail in Table I. While the outcome for the baby in the registered cases was decidedly more favorable than in the unregistered, even in the former group, if deliveries by cesarean section be excluded, the fetal mortality reached the figure of 37 per cent. If one

TABLE I. SHOWING THE FETAL MORTALITY IN 93 CASES OF TRANSVERSE PRESENTATION IN WHICH THE FETUS WEIGHED 2500 GM. OR MORE. IN THE LOWER TWO GROUPS ARE LISTED THE RESULTS, RESPECTIVELY, IN CASES WITH AND WITHOUT PRENATAL SUPERVISION

CLASSIFICATION	CASES	FETAL DEATHS	FETAL MORTALITY
Total Cases	93	44	47.2
Fetal heart heard on admission	70	21	30.0
Delivered vaginally	49	21	42.8
Delivered by cesarean section	21	0	0.0
Total Registered Cases	57	16	27.6
Fetal heart heard on admission	54	14	26.0
Delivered vaginally	38	14	37.0
Delivered by cesarean section	16	0	0.0
Total Unregistered Cases	36	28	77.0
Fetal heart heard on admission	16	7	43.0
Delivered vaginally	11	7	64.0
Delivered by cesarean section	5	0	0.0

analyzes all our vaginal deliveries in which the fetal heart had been heard on admission (considering mature babies only), the fetal death rate rises to 42.8 per cent. Martius,<sup>7</sup> who has made a thorough study of transverse presentation in Germany, states that in that country the fetal mortality from this abnormality is about 30 per cent.

These figures make it plain that, in our hands at least, transverse presentations have been attended by a fetal mortality which is higher than should be countenanced in modern obstetrics and quite naturally such results have prompted the following inquiry into the causes of fetal death in this series.

## THE CAUSES OF FETAL DEATH IN TRANSVERSE PRESENTATION

1. *Early Rupture of the Membranes.*—It may be seen in Chart II that early rupture of the membranes (prior to cervical dilatation of 7 cm.) occurred in 43 of the 60 cases in which such data were available, an incidence of over 70 per cent. It will be noted further that a definite relationship existed between the time of rupture and fetal mortality, the latter rising rapidly in those cases in which rupture occurred before the cervix was half dilated. In our cases of actual premature rupture of the membranes (that is, when rupture occurred at or before the onset of the labor), the fetal mortality was so high that it has seemed important to consider this group in more detail. Among the 13 cases so classified,

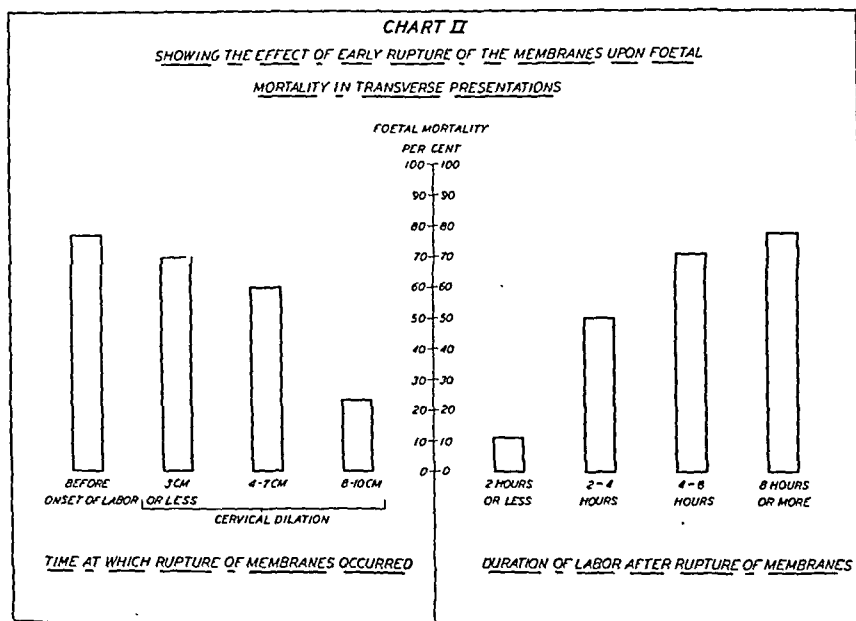


Chart 2.—The columns on the left are based on an analysis of 60 cases of transverse presentation, distributed among the four columns as follows: 13, 20, 10, and 17; those on the right are based on an analysis of 65 cases distributed as follows: 18, 10, 14, and 23.

there were 10 fetal deaths. The causes of these were as follows: prolapse of the umbilical cord, 4 cases; "hour-glass" contracture of the uterus, 3 cases; prolapse of the umbilical cord and "hour-glass" contracture of the uterus, 1 case; tetanic uterus, 1 case; and intrapartum infection, 1 case. Since the incidence of prolapse of the umbilical cord in the series as a whole was 11.2 per cent and that of contraction ring 8.2 per cent, whereas in this group it was 38.4 and 30.7 per cent, respectively, it is evident that these two complications constitute a particular menace to the fetus in cases of premature rupture of the membranes. It may be noted in passing that many cases in this group were frankly neglected ones which were sent to the hospital after many hours of labor at home.

The important rôle that early rupture of the membranes plays in causing fetal death in transverse presentations is further illustrated on the right half of Chart II, where we have shown the effect upon fetal mortality of the duration of labor after rupture of the membranes.

2. *Prolapse of the Umbilical Cord*.—This well known complication of transverse presentation occurred in 15.7 per cent of our cases in which the fetus weighed over 2500 gm. and which were delivered vaginally. With the exception of one instance, in which this accident occurred when the cervix was completely dilated, it proved fatal to the baby in every case. As mentioned previously, the likelihood of its occurrence is greater when the membranes have ruptured prematurely. Our figures suggest, moreover, that its incidence increases with multiparity, but they are not altogether conclusive on that point.

3. "*Hour-Glass*" *Contracture of the Uterus*.—By this term is meant a localized thickening of the wall of the uterus due to contraction of the circular fibers over a point of slight resistance, most frequently over a depression in the child's outline or below the presenting part. The uterine wall at the site of the contracture is therefore thicker than it is either above or below, while the wall below is neither thinned out nor distended. It may occur in the first, second or third stage of labor, does not vary in position as labor goes on, is rarely felt on abdominal examination, and is usually found in patients who are in good condition. In this abnormality, moreover, the presenting part is never found forcibly driven into the pelvis; on the other hand, the child may lie wholly or mainly above the contracture. The entity of which we are speaking, accordingly, is to be sharply differentiated from the retraction ring of Bandl (sometimes called contraction ring), which is frequently seen late during the second stage of labor in neglected cases of transverse presentation, with the fetus tightly impacted in the pelvis and the thinned out lower segment drawn closely over it.

Typical "hour-glass" contracture of the uterus was found in 7 of our 70 cases in which the fetus was mature and which were delivered vaginally, an incidence of 10 per cent. In our group of 23 cesarean sections in the series, it was found 3 additional times and was unmistakably demonstrated on the opened uterus. Indeed, one of the sections was done for this indication, since "on vaginal examination with the whole hand in the vagina, it was found that the cervix would admit the fist, which came into a dome-shaped cavity with an opening about 2.5 cm. at its apex. The margins of the ring were the thickness of the index finger and extremely resistant." (Dr. Williams.) Besides these 10 cases of "hour-glass" contracture, 2 more were met in the group of cases in which the fetus was premature, bringing the total to 12 cases, an incidence of 8.2 per cent in the 147 cases. In a quite recent case of transverse presentation not included in this series, it was found at cesarean

section that an "hour-glass" contracture of the uterus divided the uterine cavity into two compartments of almost equal size, the lower being occupied by the placenta and the upper by the fetus. This unique case will be reported in detail by E. P. H. Harrison of this Clinic.

It was characteristic of the cases of "hour-glass" contracture of the uterus seen in this series that the contractures frequently occurred in the first stage of labor and often were demonstrable surprisingly early; thus, in 3 cases they were found after less than eight hours from the onset of labor. With the exception of those patients who were delivered by cesarean section, all of them terminated with stillborn infants. The exact cause of the abnormal contracture in these patients does not seem clear, but White,<sup>8</sup> in his thorough study of the condition, points out that there is usually a history of premature rupture of the membranes and that 21.4 per cent of the reported cases have been associated with transverse presentations of the fetus.

4. *Tetanic Contraction of the Uterus.*—In contradistinction to "hour-glass" contracture of the uterus our cases of tetanic contraction in this series were observed altogether in neglected cases after many hours of labor. It was noted 6 times in the group of 70 cases in which the fetus was mature and which were delivered vaginally.

5. *Prolonged Labor.*—Prolonged labor in transverse presentations constitutes a much greater hazard for the baby than when the presentation is vertex. Thus in 34 cases in which the fetus was mature and which were delivered vaginally within twelve hours after the onset of pains, there were 11 fetal deaths, a mortality rate of 32.3 per cent; in 17 corresponding cases in which the length of labor varied between twelve and twenty-four hours, the fetal mortality rose to 64.7 per cent, while in similar patients who had been in labor more than twenty-four hours, it became 100 per cent.

6. *Border-Line Contraction of the Pelvis.*—While most of our patients with transverse presentation complicated by contracted pelvis were delivered by cesarean section, 22 patients in whom the diagonal conjugate measured between 10.0 and 11.5, were delivered per vaginam. These showed a slightly higher fetal mortality than the corresponding group of 27 cases with normal pelvis, the fetal mortality being 50.0 per cent and 37 per cent, respectively, in the two groups.

7. *Rupture of the Uterus.*—In two cases in the series the death of the fetus was the result of rupture of the uterus. In one instance spontaneous rupture occurred during the last month of pregnancy through the scar of a previous cesarean section. The other case was a neglected one in which the transverse presentation was associated with a dermoid cyst; pituitrin was administered by the private physician attending the case and rupture immediately ensued. Both mothers were treated by hysterectomy and recovered.

## TREATMENT

The advisability of preserving the bag of waters in cases of transverse presentation until complete dilatation of the cervix is, of course, a generally endorsed obstetric teaching. The present study not only attests in a convincing fashion the importance of this doctrine but indicates also the necessity of instituting active measures to prevent early rupture of the membranes in every case of this abnormality. It is our present opinion, based upon a group of cases not included in this series, that this purpose is best served by the insertion of a vaginal bag as soon as labor has become definitely established. The vaginal bag has already been recommended in transverse presentations by DeLee,<sup>9</sup> and in breech presentation by Vignes.<sup>10</sup> It lessens the likelihood of early rupture of the bag of waters by exerting counter pressure on the membranes, prevents the shoulder from becoming wedged into the pelvis, and in the event the membranes do rupture, impedes prolapse of the cord. As complete cervical dilatation is approached, the bag is usually expelled by the bulging membranes, when version and extraction may be readily effected. The vaginal bag was not employed in the series of cases reported in this paper, our previous policy having been in main an expectant one until the cervix was completely dilated.

In cases in which the membranes have ruptured early in labor or before its onset, the question of treatment is more difficult. When the undilated cervix is long and thick, the child viable and no contaminating examinations have been made, cesarean section would certainly seem to be the operation of choice, particularly if any degree of pelvic contraction is demonstrable. Naturally, many cases in this group will not be suitable for section, but we feel in general that cesarean section should receive wider use in transverse presentation, especially when the membranes rupture early; low cervical cesarean section will be the type of abdominal delivery indicated in many instances in this group. As a means of facilitating cervical dilatation in cases of transverse presentation in which the membranes have ruptured early, the intrauterine bag has proved extremely unsatisfactory in our experience; since it has repeatedly failed to effect cervical dilatation even though it has remained in place for twelve hours. Moreover, we have observed that its use in cases of transverse presentation predisposes to "hour-glass" contracture of the uterus, as well as to intrapartum infection.

We see no reason to alter our treatment of the "neglected" case. With a dead child impacted in the pelvis, decapitation is usually the only feasible procedure, although in a few desperate cases, hysterectomy on the unopened uterus must be considered because of intrapartum infection in the presence of an undilated cervix. In the rare instances in which the child is still alive, our policy has depended in large part upon the parity of the mother. If she is a multipara, cesarean section followed

by hysterectomy is usually performed, but if she is a primigravida, craniotomy is resorted to, since it does not seem justifiable in a primiparous woman to destroy all future possibility of childbearing for the sake of an infant whose chances are already jeopardized.

#### SUMMARY

1. In 147 cases of transverse presentation studied at the Johns Hopkins Hospital, there were five maternal deaths, an incidence of 3.4 per cent.

2. The chief danger to the mother in transverse presentations rests not so much in the mechanical difficulties associated with the transverse position of the fetus per se, but in certain accompanying conditions, particularly early rupture of the membranes, incomplete dilatation of the cervix, and placenta previa, complications which are often the precursors of intrapartum infection and rupture of the uterus.

3. The fetal mortality in the registered cases in this series, considering only cases in which the fetus weighed 2500 gm. or more, was 27.6 per cent, while if the cases delivered by cesarean section be excluded from this group, it rose to 37.0 per cent.

4. The underlying factors in the causation of fetal death were early rupture of the membranes, slow and incomplete dilatation of the cervix, prolapse of the umbilical cord and "hour-glass" contracture of the uterus.

5. "Hour-glass" contracture of the uterus was observed in 8.2 per cent of the 147 cases, often occurred early in labor, and constituted an important cause of fetal death.

6. Active measures to prevent early rupture of the membranes should be instituted in every case of transverse presentation, and to this end the use of the vaginal bag is recommended.

7. In certain cases of transverse presentation, particularly when the membranes have ruptured early, the judicious employment of cesarean section is advised.

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# OCCIPITOPOSTERIOR POSITION AND THE TRANSVERSELY CONTRACTED PELVIS

## A PRELIMINARY REPORT

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IN A recent paper entitled "The Shortening of the Transverse Diameter of the Superior Strait and Its Clinical Significance,"<sup>1</sup> I pointed out first, the importance of x-ray pelvimetry of the superior strait; second, the fact that only by some such method could the transverse diameter of the superior strait be accurately estimated; third, that external pelvic measurements, as far as estimating accurately this diameter, are practically valueless; and finally, the importance, particularly in the simple flat pelvis and the generally contracted pelvis, of the transverse diameter of the superior strait.

During the past year, I have continued my studies, paying particular attention to the relationship between the relative or real shortening of the transverse diameter and the course of labor. In the present paper, the findings in 16 consecutive cases of such shortening are reviewed; and when it is realized that in each of these 16 consecutive cases an occipitoposterior or an occipitotransverse position was present at some time during the labor, it will be seen that I have not underestimated the importance of obtaining knowledge of this diameter. In all of the cases presented, x-ray pelvimetry of the superior strait was performed either prior to or following labor. In those cases where x-ray pelvimetry was done before labor, and a relative or real shortening of the transverse diameter found, a subsequent occipitoposterior or occipitotransverse was noted during labor; and in those cases which showed an occipitoposterior position during labor, and in which x-ray pelvimetry was done postpartum, in each case a relative or real shortening of the transverse diameter was found.

I might at this point explain what is meant by relative and real shortening of the transverse diameter of the superior strait. When this diameter is definitely shorter than that of the normal measurement (12.5 to 13.5 cm.), real shortening is designated. However, when the normal relationship between the transverse and anteroposterior diameter is disturbed, as is shown in Cases 3 and 7, I refer to such distortion as relative shortening. That is, when the transverse diameter approaches, is equal to, or even less than the anteroposterior diameter.

The present communication, which is a preliminary report, is divided into two parts, first, the reports of 16 consecutive cases, with their superior strait pelvigrams, and second, a discussion of the findings.

## CASE REPORTS

CASE 1.—Primipara, aged twenty-three years. Sp. 23, Cr. 26, Tro. 28.5, Ext. Conj. 18. Vaginal examination showed L.O.P. in deep position. At the end of sixteen hours, labor was ended by forceps, and a 2920 gm. baby delivered. True a.p. diameter of inlet 11 cm., transverse 11.75 cm.

*Comment.*—Disproportion suspected because of small measurements and x-ray pelvimetry done one week prior to delivery. A typical small round pelvis, due to relative shortening of the transverse diameter. Occipitoposterior was predicted before engagement.

CASE 2.—Primipara, aged twenty-six years. Sp. 24, Cr. 26, Tro. 28, Ext. Conj. 18.5. Early in labor, vaginal examination showed R.O.P. position. A 2738 gm. baby was delivered. True a.p. diameter of inlet 10.75 cm., transverse 11 cm.

*Comment.*—X-ray pelvimetry done at onset of labor before engagement and occipitoposterior position predicted.

CASE 3.—Primipara, aged twenty-five years. Sp. 27, Cr. 29, Tro. 34, Ext. Conj. 22, diagonal conjugate not reached. Persistent R.O.P. delivered as O.P. after a six-hour labor and a second stage of one-half hour. A 3210 gm. baby spontaneously delivered. True a.p. diameter of inlet 13.5 cm., transverse 13.25 cm.

*Comment.*—Large woman, with justomajor measurements. Without x-ray diagnosis, no such shortening would have been discovered. X-ray pelvimetry was done in this case three months postpartum, because from our experience the shortening of the transverse diameter was suspected.

CASE 4.—Primipara, aged nineteen years, colored. Sp. 23, Cr. 24, Tro. 27, Ext. Conj. 18.5, C.D. 11.5. Diagnosis of R.O.P. made by vaginal examination during first stage of labor. Normal, spontaneous delivery in R.O.A. A 2835 gm. baby. X-ray pelvimetry performed at sixth month of pregnancy, because of small external measurements. Spontaneous delivery expected from findings. True a.p. diameter of inlet 10.5 cm., transverse 11 cm.

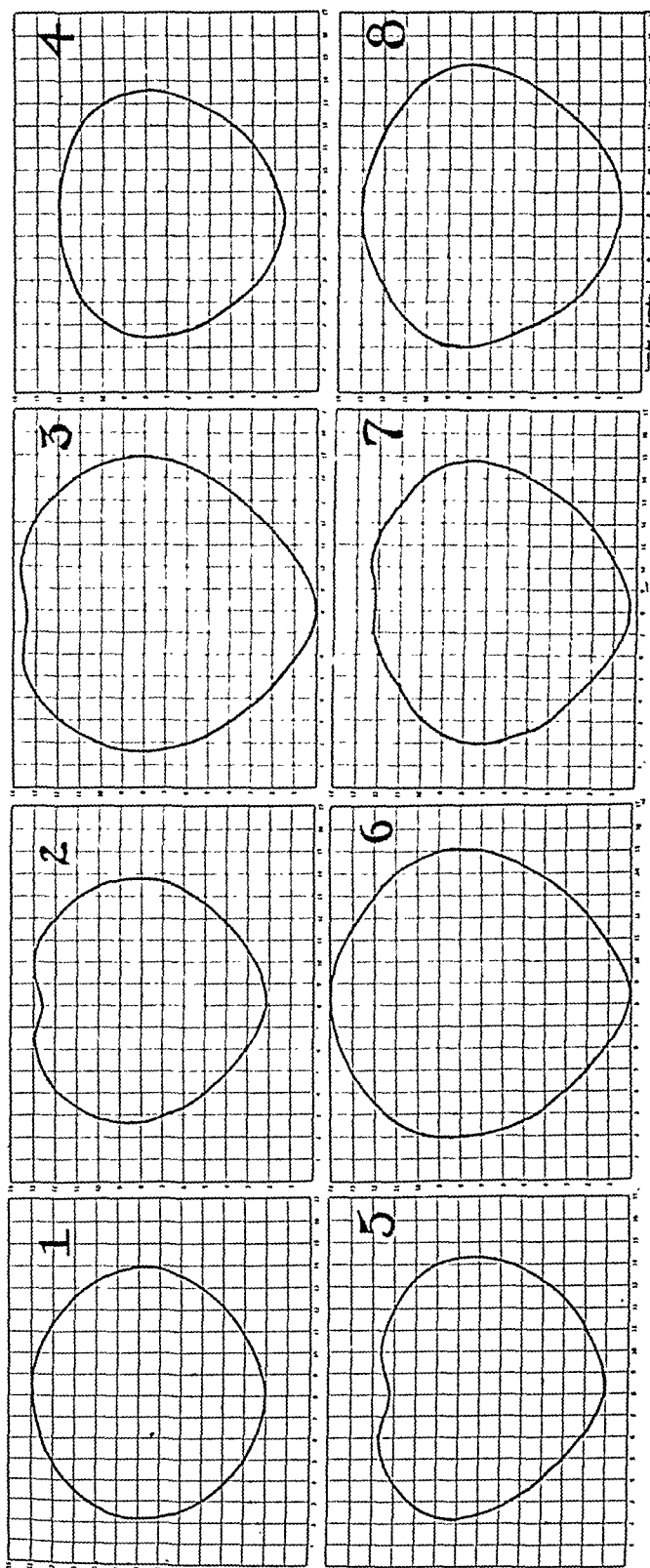
CASE 5.—Primipara, aged seventeen years. Sp. 25.5, Cr. 27.5, Tro. 32, Ext. Conj. 19.5. Postpartum left oblique 21.0, right oblique 22.5, diag. conj. 11 plus. Vaginal examination during labor showed persistent right occipitoposterior, and at the end of twenty-seven and one-half hours of labor, a Seanzoni double application of forceps was done and a 3610 gm. baby delivered. True a.p. diameter of inlet 10.25 cm., transverse 12 cm.

*Comment.*—X-ray pelvimetry taken postpartum, interesting asymmetry found, which was not suspected. It is probable that the lessening of the available room at the right anterior half of the superior strait caused a right posterior rotation of the occiput. If we compare the right half of this superior strait to the left half, we see that owing to the present asymmetry, the right half of the pelvis contains approximately 46 square centimeters, while the left half, which is normal in appearance, contains 53 square centimeters. If the fetus had presented with the occiput in the left half of the pelvis, is it reasonable to assume that we might have had an L.O.A. position early in labor?

CASE 6.—Primipara, aged twenty-nine years. Sp. 26, Cr. 29, Tro. 31, Ext. Conj. 21, Diag. Conj. not reached. Vaginal examination showed a persistent right occipitoposterior at the end of eleven hours of labor, and a low forceps was performed, delivering a 3425 gm. baby. True a.p. diameter of inlet 14 cm., transverse 13 cm.

*Comment.*—This pelvis is not unlike that of Case 3. Large external measurements and because of the persistent occipitoposterior transverse shortening not suspected until x-ray pelvimetry was done. Here again is the justomajor type of pelvis in which occipitoposterior would not have been considered from external measurements alone. Nevertheless, the transverse diameter is actually 1 cm. shorter than the anteroposterior.





CASE 7.—Primipara, aged twenty-three years. Sp. 27, Cr. 29, Tro. 31, Ext. Conj. 21.5, Diag. Conj. not reached. A twenty-seven-hour labor terminated by double application of forceps for R.O.P. position. One and one-half hour second stage showed no advance. A 3570 gm. baby delivered. True a.p. diameter of inlet 12 cm., transverse 12.75.

*Comment.*—X-ray pelvimetry taken postpartum showed relative shortening of the transverse diameter.

CASE 8.—Primipara, aged eighteen years. Sp. 26, Cr. 27.5, Tro. 32.5, Ext. Conj. 20.5, Diag. Conj. not reached. Left occipitoposterior was found at term and labor showed rotation from this position to the left occipitoanterior with spontaneous delivery of a 3485 gm. baby. True a.p. diameter of inlet 12 cm., transverse 12.75 cm.

*Comment.*—Postpartum x-ray showed a relatively shortened transverse diameter in a pelvis with ample room in all other diameters.

CASE 9.—Primipara, aged twenty-five years, patient of Dr. L. Sp. 20, Cr. 26, Tro. 28, Ext. Conj. 21, Diag. Conj. not reached. Antepartum x-ray pelvimetry showed a remarkable transverse shortening, which was totally unsuspected from external measurements. Posterior position of the occiput predicted after viewing the pelvi-gram, and the patient delivered by forceps from R.O.P. 3100 gm. baby. True a.p. diameter of inlet 12 cm., transverse 11 cm.

CASE 10.—Primipara, aged nineteen years. Sp. 23, Cr. 25.5, Tro. 30, Ext. Conj. 17.5, Diag. Conj. not reached. Low transverse arrest after one and one-half hours of second stage. A 3285 gm. baby delivered with forceps from R.O.T. True a.p. diameter of inlet 10.75 cm., transverse 11.75 cm.

*Comment.*—Typical small round pelvis with common sequelae noted at labor. Although this patient was not examined early in labor, but was delivered for transverse arrest, I think we may assume that the transverse position was preceded by a right occipitoposterior earlier in labor.

CASE 11.—Primipara, aged twenty-nine years. Sp. 27, Cr. 28.75, Tro. 31, Ext. Conj. 20.5, Diag. Conj. not reached. Persistent right occipitoposterior, delivered by low forceps after a three and one-half hour second stage, and a total labor of nine and one-half hours. A 3965 gm. baby. True a.p. diameter of inlet 13.75 cm., transverse 11.25 cm.

*Comment.*—This case shows a very remarkable shortening of the transverse diameter.

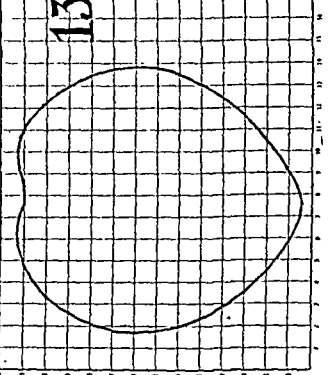
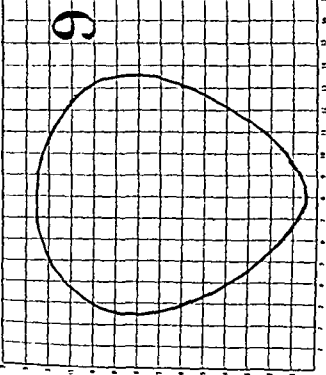
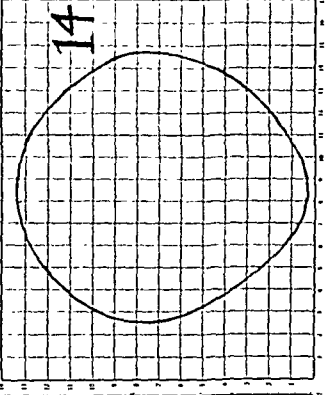
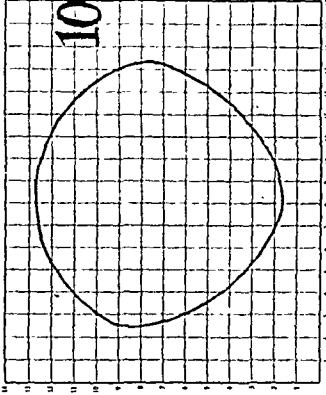
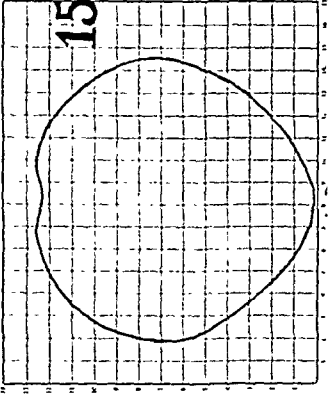
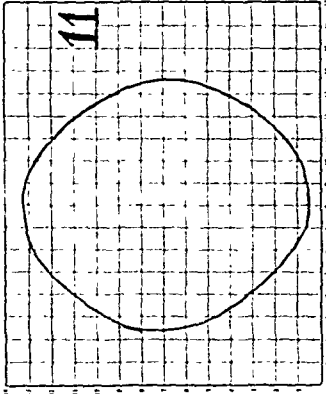
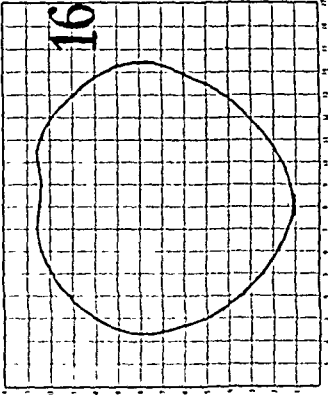
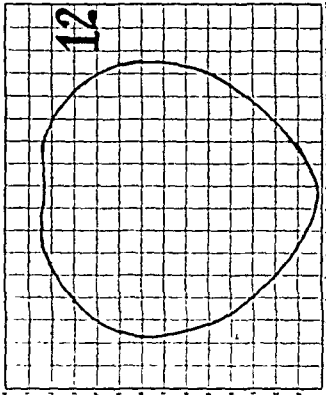
CASE 12.—Para iv, aged thirty-three years, patient of Dr. L. Sp. 26, Cr. 28, Tro. 30, Ext. Conj. 19. Right occipitoposterior. Diagnosis early in labor by vaginal examination. Spontaneous delivery of a 3116 gm. baby, after one and one-half hour labor. True a.p. diameter of inlet 12 cm., transverse diameter 12 cm. Previous history in this case shows: 1929, R.O.P., one and three-fourths hour labor and 3626 gm. baby; 1929, R.O.P., seven-hour labor, 3510 gm. baby; 1926, R.O.A., nineteen-hour labor, 2762 gm. baby, mid forceps.

*Comment.*—This case is extremely interesting in that a small baby of 2762 gm. is said to have been delivered from R.O.A. by mid forceps, in her first labor.

CASE 13.—Patient Dr. M. Primipara, aged thirty years. Sp. 24, Cr. 28, Tro. 32, Ext. Conj. 19, Diag. Conj. not reached. At onset of labor showed R.O.P. position. A 3330 gm. baby delivered. True a.p. diameter 12.5 cm., transverse 12 cm.

CASE 14.—Primipara, aged twenty-four years. Patient of Dr. R. F. R. Sp. 24, Cr. 29, Tro. 30, Ext. Conj. 18.5, Diag. Conj. not reached. At the beginning of labor showed an occipitoposterior position. A 3890 gm. baby delivered. True a.p. diameter 13 cm., transverse 12.25 cm.

CASE 15.—Para i, aged forty years. Previous history not obtainable. Sp. 21, Cr. 23, Tro. 30, Ext. Conj. 29, Diag. Conj. not reached, Bituberal 9. Vaginal exami-



nation during the second stage showed a right occipitotransverse, and the patient subsequently delivered spontaneously from R.O.A., 2360 gm. baby. True a.p. diameter of inlet 12.25 cm., transverse 12.50 cm.

*Comment.*—This patient shows a relative shortening of the transverse diameter. This premature baby was noticed first as an R.O.T. Whether this was preceded by R.O.P., it is impossible to say. Nevertheless, with a full-term baby of 3000 gm. or more, I feel that the occiput would probably enter the superior strait either in the right or left posterior position.

CASE 16.—Primipara, aged twenty-one years. Sp. 23, Cr. 26, Tro. 27, Ext. Conj. 18.5, Diag. Conj. not reached. Bituberal 9. At the end of a fifty-three-hour labor, vaginal examination showed transverse arrest and mid forceps delivery of a 2250 gm. baby from L.O.T. True a.p. diameter 11.5 cm., transverse 12 cm.

*Comment.*—This situation is similar to that in Case 15. I am certain that the relative shortening in both of these cases had a great deal to do with the transverse arrest; and in this latter case, from my experience, I am of the opinion that the head entered the pelvis in the L.O.P. position.

In summarizing the 16 cases of occipitoposterior and transverse arrest which have been brought consecutively to my attention, one is immediately impressed with the 100 per cent incidence of pelvis in which the superior straits do not conform to our conception of the normal. Furthermore, transverse contractions of the pelvic inlet either real or relative are far more frequent than hitherto supposed, and have a most important place in the etiology of occipitoposterior positions. In this small series, the types found divide themselves into two general groups; first, the so-called small round, or generally contracted pelvis, which are represented by Cases 1, 2, 4, 10, and 16; and second, those pelvis which are normal except for a relative shortening of the transverse diameter of the superior strait, Cases 3, 6, 11, 13, and 14.

The study as a whole proves again to my mind that the usual external pelvic measurements as a guide to actual superior strait measurements, are in many cases fallacious and may be very misleading. I have performed x-ray pelvimetry in this clinic for a period of nearly twelve years, and at the present time am so impressed with its value that I am of the opinion that x-ray pelvimetry should be an essential part of the prenatal examination of every primiparous woman. While this preliminary series is small, yet it seems beyond doubt that the further study which is now being made not only will demonstrate many interesting facts with regard to the superior strait but may solve the etiologic factors concerned in the production in the majority of instances of occipitoposterior position. From the present small series, it appears that when the transverse diameter of the pelvis is actually or relatively shortened, this shortening restricts the space in the anterior half of the pelvis much more than it does that of the posterior half; and for this reason, it appears that at the beginning of labor, when the head descends, the occiput is forced to assume a posterior course. Furthermore, I am more and more impressed in my studies both in x-ray pelvimetry of the superior strait and in fetal cephalometry, with the fact that in the

majority of cases of labor in normal pelvis the head first dips into the superior strait before engagement with the occipitofrontal diameter of the fetal head parallel to one or the other transverse diameters of the superior strait, and not parallel to one or the other oblique diameters, as is generally taught. Thus, before deep engagement of the fetal head, I think that we must revise our ideas of fetal position in utero before labor and employ more often the terms "left occiput transverse" or "right occiput transverse" as the case may be.

I realize that one is prone to make exaggerated statements regarding studies in which one is particularly interested. Nevertheless, I am thoroughly convinced of our woeful ignorance regarding the diameters of the superior strait of the bony pelvis, as gathered from the usual methods of pelvimetry. I have pointed out before that until the advent of x-ray methods in pelvimetry, there was no noteworthy advance in our methods of diagnosis of superior strait contractions since the time that William Smellie first described the estimation of the diagonal conjugate.

The rôle which ignorance plays in our alarming obstetric statistics will certainly be less when men who deliver women possess accurate knowledge of the bony pelvis of their patients. Every pregnant woman has a right to expect every scientific aid that can be given to safeguard her own and her baby's life and as a final word, I repeat once more that regardless of external measurements, x-ray pelvimetry should be an essential part of the prenatal examination of every primiparous woman.

#### REFERENCE

1. *Thoms, H.*: AM. J. OBST. & GYNEC. 19: 539, 1930.

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**Consoli:** Tuberculous Heredity. Arch. Ostet. e Ginec. 17: 207, 1930.

The author investigated on guinea pigs the transplacental transmission of tuberculosis. These researches lead him to admit the transplacental passage of the T. B. virus in a filtrable form as possible but not very frequent. The frequency of such passage seems to be dependent upon the entity of tissue lesions.

Only in one guinea pig was positively ascertained a transplacental transmission.

SYDNEY S. SCHOCHET.

JULIUS E. LACKNER.

**Klemperer, Felix:** Tuberculosis and Pregnancy. Ztschr. f. Geburtsh. u. Gynäk. 96: 1, 1929.

The author feels that it is impossible to give any data which will show the effect of pregnancy on the course of tuberculosis. Earliest possible termination of the pregnancy does not cure the disease, but eliminates baneful effects of the pregnancy and facilitates the treatment. He also feels that each case must be individualized and that the medical and social conditions determine whether or not a given pregnancy should be interrupted. Placing of the patient in a sanatorium greatly increases the chances of recovery and often makes unnecessary a therapeutic abortion.

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# LEUCOPLAKIA OF THE CERVIX UTERI\*

## A MANIFESTATION OF EARLY MALIGNANT CHANGE?

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**L**EUCOPLAKIA of the cervix uteri, as a probable manifestation of cancer in its earliest form, has received practically no consideration in the English literature. This is not surprising, since leucoplakic plaques heretofore described were either large enough to be seen with the unaided eye, a rarity, or represented mere chance histologic observations. An occasional mention, or a case report, is found, as that by L'Esperance,<sup>2</sup> who, in a consideration of early cervical cancer, mentions an instance of leucoplakia in a patient "apparently" afflicted with congenital syphilis. Emil Ries<sup>15</sup> has recently called attention to this lesion as probably a "carcinad" manifestation. Stone<sup>17</sup> mentions two cases of leucoplakia, which were not recognized clinically, where histologic examination showed changes not altogether conclusive of superficial malignancy without invasion. The importance of syphilitic lesions of the cervix as a possible predisposing factor in the cause of malignant change is now well recognized, and in this country has been especially emphasized by Gellhorn.<sup>6</sup> However, in this presentation, we are not concerned with lesions secondary to syphilis.

Hinselmann,<sup>7,9</sup> in 1927, was the first to call attention to small white areas (leucoplakia) on the cervix which generally escaped observation by ordinary speculum examination, but were rendered plainly visible under the low power magnification of a dissecting prism. Histologic examination of these areas generally revealed a picture compatible with leucoplakia, in which the finer histologic details varied from mere epithelial hyperplasia to those changes ordinarily only associated with the cytology of malignancy but without invasion.

### HISTORICAL

Probably the first carefully described instance of leucoplakia of the cervix was given by d'Hotman de Villiers and Thérèse.<sup>10</sup> This concerned a parous woman, forty-one years old, who was seen two years prior to the time of their report. Speculum examination revealed a small pearly white plaque the size of a "15 centime piece" on the middle portion of the inferior aspect of the cervix. In May, 1895, the patient again came under observation and the plaque then was seen to gradually enlarge so that in one month it doubled its size. The authors considered the plaque analogous to the cancerous plaques sometimes seen on the tongues of smokers, and therefore performed an amputation of the cervix. Histologic examination showed a superficial horny layer

\*Read at a meeting of the Portland Society of Obstetricians and Gynecologists, April 27, 1932.

of epithelium. Beneath this the malpighian layer was thickened and in areas epithelial changes suggestive of early epithelial pearl formation were seen. No mitotic figures were seen, and there was no invasion of the underlying stroma.

Verdalle,<sup>19</sup> in 1903, reported three cases of leucoplakia of the cervix uteri which apparently developed into unmistakable cancer. The one case personally observed by Verdalle was in a fifty-year-old parous woman, probably syphilitic, who complained of menstrual irregularity. Two pearl white plaques were seen on the anterior lip of the cervix. One plaque was the size of a "2 franc" piece and the other the size of "50 centimes." They had been there for several years according to the information given Verdalle. Two years later the patient returned and at this time presented an advanced cancer of the cervix uteri. It is obvious from Verdalle's careful account that it could not be stated whether the carcinoma actually developed on the site of the previously observed leucoplakic area or on some other area of the cervix. All that can be concluded is that a cancer developed on a cervix which two years previously showed unmistakable evidence of leucoplakia.

The other cases mentioned by Verdalle are those of Labadie-Lagrave. One of these occurred in a woman fifty years of age who had two leucoplakic plaques on the cervix. A cancer of the cervix invading the corpus uteri was observed eight years later in this patient. The other case was that of a woman who had a leucoplakia on the inferior lip of the cervix, which several years later became involved in cancer. In none of these instances is there any record to shew that the observations were spaced sufficiently closely to allow the conclusion that the development of cancer was primarily on the base of a previously observed leucoplakia.

Von Franqué<sup>4</sup> has long felt that cancer of the portio cervicis probably manifests itself first as a leucoplakic change, and, conversely, that certain leucoplakic plaques are destined to eventually become carcinomas. He mentions a case reported by himself in 1899 concerning a parous woman fifty years of age. Examination revealed white spots on the portio cervicis which on histologic examination merely showed some thickening of the epithelium. The patient was under observation for years and on one visit an ulcer, the size of a "mark," was seen. Examination disclosed this to be a cancer that had invaded "hardly a few millimeters."

Another case reported by von Franqué is that of a woman forty-five years of age who was examined for the first time in 1896. Three years later leucoplakia of the cervix was observed. Five years after this the patient was seen by another physician who reported a well-developed cancer on the anterior lip. The patient was again seen some time later by von Franqué who confirmed the diagnosis and operated.

From 1907 to 1927, we have found no references, except one by Hofbauer,<sup>20</sup> that concern themselves primarily with the subject of leucoplakia of the cervix.

#### RECENT CONTRIBUTIONS

Interest in the subject of cervical leucoplakia is again manifest in the German literature due to the efforts of Hinselmann. As previously noted Hinselmann ingeniously employed a dissecting prism with which to inspect the cervix. Under a magnification of 10 to 15 diameters, Hinselmann observed, in some patients, small white spots on the portio cervicis which escaped recognition entirely by the unaided eye. These white spots were found to be areas characterized by rather definite epithelial changes and, in fact, were minute leucoplakic areas. The first two cases reported by Hinselmann<sup>7</sup> were rather extensive and

could be seen without magnification. The specimens were examined by von Franqué<sup>2</sup> who considered the histologic picture pathognomonic of beginning cancer before the stage of invasion. Perusal of the description and illustrations would convince one familiar with gynecologic pathology that the *cytologic* changes described are those which one associates with cancer of the cervix. In both cases the leucoplakic areas began as an abrupt change from normal cervical stratified epithelium to a stratified epithelium which had lost its layer formation. The lowermost layers (the basal layer and stratum mucosum) showed hyperplasia with closely placed, pyknotic nuclei. Large spindle-shaped cells were present, some with their long axes directed obliquely to the basal membrane which in turn had lost its identity. A stratum corneum was absent and mitotic figures were frequent.

In general, but not always,<sup>3</sup> leucoplakic plaques of the cervix uteri occur on cervixes where there is an area of altered epithelization as characterized grossly by a circumstrial vermilion halo which is often in-



Fig. 1.—Extensive leucoplakic alteration encircling the cervix. External os is at *a*. (Hinselmann-Zentralbl. f. Gynäk., April, 1927.)

correctly referred to as an “erosion.” The leucoplakic area, according to Hinselmann, occurs most commonly on the transition zone where columnar and stratified epithelium meet.

The leucoplakic plaques appear as white or pearl white, slightly raised, circumscribed areas of varying size against a pink or pale pink background. Fig. 1 illustrates an extensive and unusual variety while Fig. 2 illustrates a smaller and more common type of leucoplakia. The majority of plaques occur singly but they may and do occur in varying numbers. They vary considerably in size,<sup>12</sup> but most of them measure less than 5 mm. in their largest dimension, while many appear as mere pin-point areas. Hinselmann also describes a checkered variety wherein the leucoplakic areas occur as white polyhedral patches which are surrounded by pink lines of undamaged cervical epithelium. We have observed such areas on several occasions, but have not studied them histologically.



The cervix about the external os, when viewed under a magnification of 10 to 15 diameters, presents some rather bizarre appearances. One of these is the discharge of secretion from glands which open onto the portio and the other is an occasional small yellowish gray elevated area that represents a plugged cervical gland.

According to both Hinselmann<sup>13</sup> and Rogge<sup>16</sup> a leucoplakia may be visible on one occasion, later lose its distinguishing color and reappear on a subsequent examination. This we have also observed.

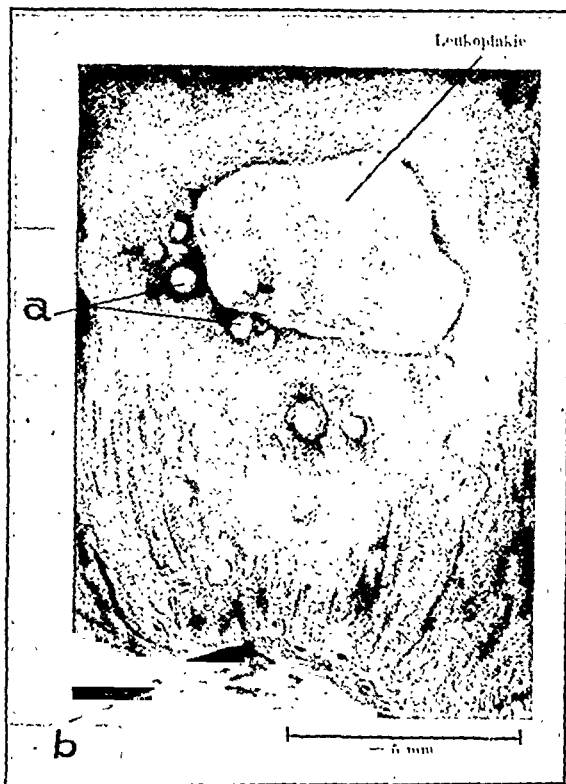


Fig. 2.—Leucoplakia under 5½ diameters magnification. At *a* are minute white areas that represent plugged orifices of cervical glands. External os at *b*. (Hinselmann-Zentralbl. f. Gynäk., 1927.)

#### HISTOLOGY

Leucoplakic plaques, leaving aside for the moment the finer cytologic variations, generally show an abrupt transition at the point where normal epithelium ends and the leucoplakia begins. Fig. 3 shows this clearly. The epithelium of the leucoplakic area is more compact, though not necessarily thicker than normal, the epidermal papillae generally are more pronounced and there is a tendency for a hyperplasia of the cells of the basal layer and stratum mucosum, so that normal layer formation is lost. Usually a stratum corneum, and, less commonly, a zone of granular cells of varying thickness, representing a stratum granulosum, are present. Von Franqué believes a hyperplastic stratum mucosum is suf-

ficient to produce the white appearance of a leucoplakia and that neither a stratum corneum nor granulosum are essential.

In addition to the above description Hinselmann considers a sub-epithelial round cell infiltration as part of the histologic picture of leucoplakia. As a matter of fact the foregoing description does not apply

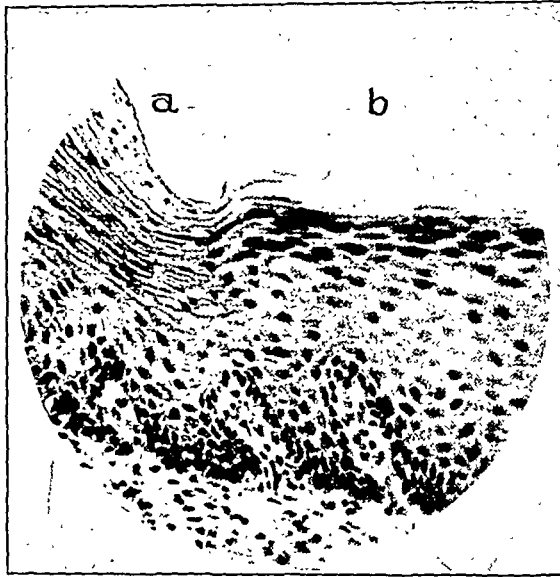


Fig. 3.—Photomicrograph of margin of leucoplakia. Under *a* the epithelium appears essentially normal and shows various cell layers. Note sudden transition to *b* which represents the leucoplakia. Here cells are compact, spinal cell layer is not discernible and the dark appearing cells near the surface represent a stratum granulosum. (Esser-Virchow's Arch., 1928.)

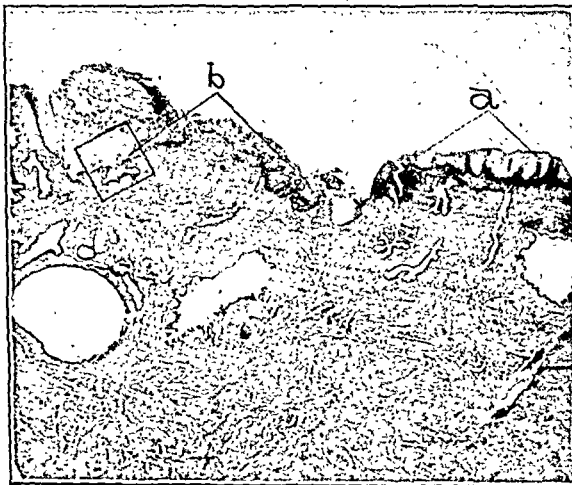


Fig. 4.—At *a* is essentially normal cervical epithelium with some underlying glands. The depression between areas *a* and *b* is lined by a single layer of columnar epithelium and represents portion of a cervical gland. Epithelium at *b* shows pronounced alteration. The papillae are very irregular, show a tendency to clubbing, and apparently are increased in number. In right half of *b* an occasional area shows some stratum corneum and a few superficial granular cells are present suggestive of a fragment of stratum granulosum. Layer formation is not entirely lost, for some areas show a thin layer of spinal cells. Generally there is marked irregularity in size, shape, and staining reaction of the cells. There are numerous spindle cells, mitotic figures and some epithelial whorls. Left half of *b* shows gland partially filled with stratified epithelium.

to all leucoplakic areas. Some do not show a definite thickening of the epithelium as compared with the normal. Probably the most constant finding is the proliferation of the cells in the basal portion of the stratum mucosum, a well defined subepithelial round cell infiltration and an in-



Fig. 5.—From right half of *b* Fig. 4. *a* is mitotic figure. At *b* is a stratum corneum which photographs very indistinctly. At *c* is a superficial epithelial whorl.

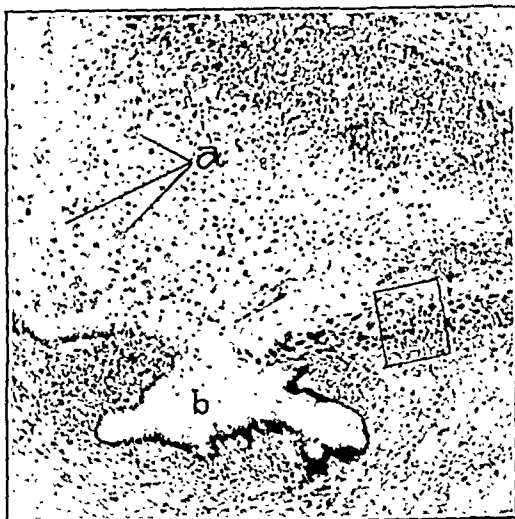


Fig. 6.—From blocked area in Fig. 4. At *a* are large multinuclear cells. *b* remains of a cervical gland. The majority of the cells in this area are of the spinal cell type but show most unusual irregularity in shape and staining reaction. Mitoses are present.

creased irregularity in the basal zone where it rests on the tunica propria. A sharp zone of transition from the normal to the abnormal is also a fairly regular observation.

Leucoplakic plaques, however, all show some histologic abnormality to

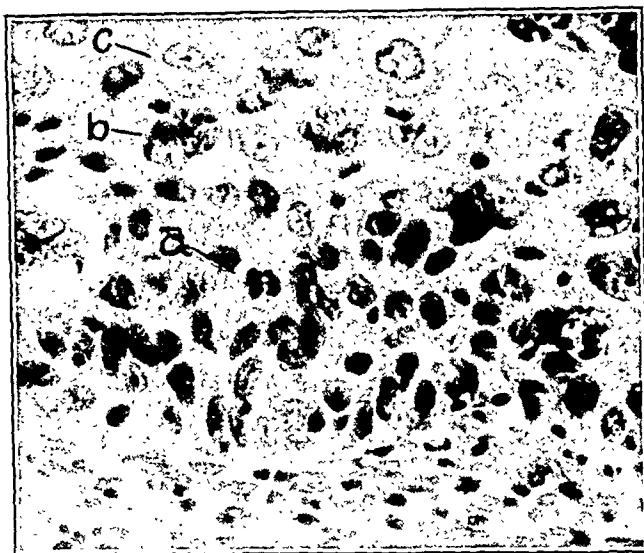


Fig. 7.—From blocked area in Fig. 6. Shows marked cellular irregularity. Mitotic figure at *a*; huge, coarsely granular oval cell at *b*; large multinuclear cell at *c*.



Fig. 8.—Healed cervical injury. *a*, hyperplastic epithelium with uniform cells, regular layer formation, no mitoses. *b*, cervical glands one of which is partially lined with stratified epithelium. *x*, cervical canal.

account for their white color. This may be due to (1) a hyperplastic epithelium (stratum mucosum); (2) a stratum corneum and a possible stratum granulosum in the absence of pronounced hyperplasia of the mucosum; or (3) a combination of 1 and 2.

The foregoing observations would be more or less academic were it not for the disturbing fact that in numerous leucoplakic areas the hyperplastic epithelium shows a most disordered cytology. This may be so pronounced that the epithelial cells in addition to their more or less customary loss of well-differentiated layers, have become irregular in size, shape, and staining reaction. There is loss of polarity, spindle cells may be found at almost any level, while large polynuclear cells, multinucleo-

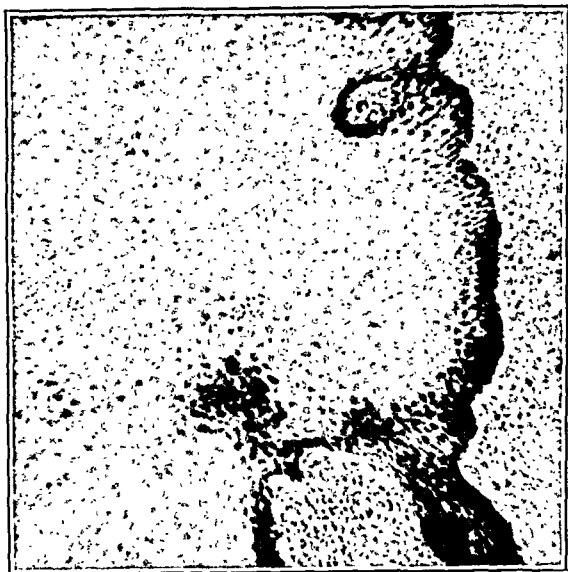


Fig. 9.—High power of blocked area in Fig. 8. Note uniform size, shape and staining reaction of cells.

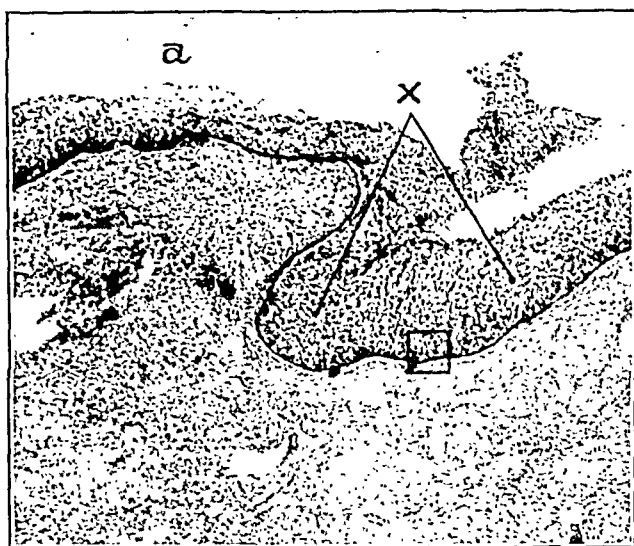


Fig. 10.—Section from edge of bona fide early cancer which in areas, not here illustrated, showed lymphatic invasion for depth of 2 mm. *a*, normal stratified epithelium which undergoes rather sudden transition. *x*, hyperplastic epithelium composed almost entirely of spindle cells of varying size with numerous mitoses. This area is histologically similar to cancer cell nests seen in other parts of specimen and is shown for comparison with Fig. 12. (*Johns Hopkins Hosp. Bull.*, June, 1922.)

lated nuclei, mitotic figures and epithelial whorls may be present. In other words the cytology is that commonly encountered in a well-developed cancer of the cervix and a leucoplakia presenting such a histologic picture lacks one anatomic requisite, invasion, to make it a carcinoma. Figs. 4, 5, 6, and 7 from a case of ours show all these cytologic characteristics.

For the sake of contrast, Figs. 8 and 9 show the histology commonly encountered in an area of epithelial hyperplasia from a cervical scar. To further show the histologic similarity between a bona fide early cancer of the cervix<sup>14</sup> whose deepest demonstrable invasion is 2 millimeters and an area of epithelial change that possesses all the recognizable cellular

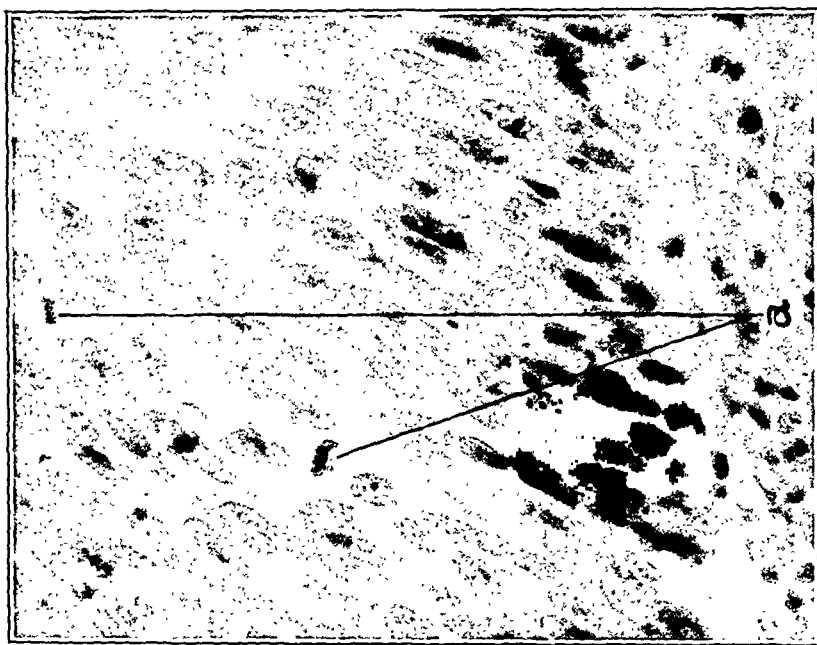


Fig. 11.—From blocked area in Fig. 10. Note large spindle cells and mitotic figures at *a* which have been retouched. (*Johns Hopkins Hosp. Bull.*, June, 1922.)

earmarks of malignancy without invasion, we present Figs. 10 to 13 whose legends are self-explanatory.

In brief the histologic picture presented by some leucoplakias as represented by Figs. 4 to 7 are changes which we associate with malignancy of the cervix uteri, and if the term precancerous is permissible, it might be applied here. There is rather general agreement on this point by pathologists and gynecologists conversant with the histologic changes peculiar to the female generative tract. On the basis of such findings, we would call attention to the stand taken by Cullen in this country concerning the mere presence of mitoses in cervical epithelium. He has repeatedly expressed himself to the effect that in the normal course of events, mitoses must occur in the cervical epithelium for the processes of growth and repair. The fact remains, nevertheless, that in routine his-

tologic studies of the cervix uteri, epithelial mitoses are so uncommon that they are practically never encountered except where malignancy exists.<sup>1</sup>

On the basis of the above described histologic changes that occur in some leucoplakias, and using as additional proof the observations of von Franqué, de Villiers et Thérèse, and Verdalle, the conclusion is reached that cervical leucoplakias at times develop into unquestioned carcinomas. While this may be true, still for the establishment of irrevocable proof, we believe it will be necessary first to observe a leucoplakia and if the lesion is large enough, obtain histologic evidence by biopsy of its nature. It would then seem necessary to keep the patient under observation until such a time as the remaining *leucoplakic plaque itself* began to show

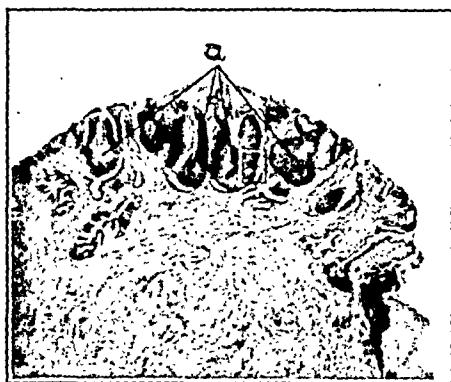


Fig. 12.



Fig. 13.

Fig. 12.—From a minute bleeding cervical area which shows superficial loss of substance and presence of superficial capillaries which account for bleeding. *a*, compact epithelial cell nests occupying gland lumina. Cells are spindle-shaped and oval, mitoses are numerous and these areas are histologically similar to outspoken cancer areas seen in specimen from which section in Fig. 10 is taken. Cytologically this is cancer. Clinically this was a small bleeding erosion.

Fig. 13.—From blocked area in Fig. 12. Magnification not as great as in Fig. 11, however, histology is quite similar. Note mitotic figures at *a* and lumen of neighboring gland at *b*. Mitotic figures retouched.

changes that might be construed as malignant. If the radically removed specimen then showed histologic evidence in the leucoplakic area of early but unmistakable carcinomatous invasion then there could be no doubt that leucoplakias may become true carcinomas.

It is self-evident that the presence of a superficial histologically malignant alteration of the cervical epithelium as seen in some leucoplakias is not proof that the process may go on to invasion and therefore obvious malignancy. We are also loath to accept the oft-quoted observations of von Franqué, d'Hotman, de Villiers et Thérèse, and of Verdalle as conclusive evidence that cervical leucoplakia may become carcinomatous. The authors mentioned saw cancer develop on cervixes where leucoplakia had been previously noted. However, they do not specifically mention that the cancers began exactly on the site of a previously ob-

served and charted leucoplakia. In fact, this would have been impossible, for, with the exception of von Franqué's first case, at the time the patients presented themselves with cancer the process was so well advanced that it would have been impossible to say whether it actually arose on the base of a leucoplakic plaque or from some other surface of the cervix.

These remarks should not be construed as mitigating the surpassing importance of Hinselmann's contribution to the recognition of small leucoplakic areas by means of low power magnification nor the observation that many of these lesions show cytologic changes which we associate with malignancy even in the absence of invasion.

#### SUMMARY AND CONCLUSION

Leucoplakia of the cervix uteri as a clinical and pathologic entity is a lesion heretofore infrequently reported.

The epithelial changes in some leucoplakic plaques have all the cytologic characteristics of cancer but lack the attribute of invasion (heterotopia).

Observers believe and cite evidence that some leucoplakias of the cervix provide the basis for subsequent cancer development. This is a reasonable point of view, but we do not believe that evidence available for its support is conclusive.

We believe Hinselmann's work is of surpassing importance for cancer prophylaxis, and worthy of general recognition. The recognition of small leucoplakic areas on the cervix may well afford the clue to cancer in its earliest form in this situation and at a time when its eradication would be relatively simple.

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# ABDOMINAL CESAREAN SECTIONS IN DETROIT IN 1930\*

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FIVE years have elapsed since Welz's report on the abdominal cesarean section done in Detroit, and in the light of his none too optimistic paper another attempt will be made to analyze the cases occurring during the year 1930.

In the year 1930 the total births for the City were 33,988 of which 14,836 occurred in hospitals. Five hospitals: Women's, Providence, Crittenden, Harper, and Herman Kiefer, each had 1,000 or more deliveries during the year. In all 125 abdominal sections were performed among 9,584 cases, an incidence of 1 in 76. In eleven hospitals in which there were less than 1,000 deliveries during the year, there were 78 sections in 4,252 cases, an incidence of 1 in 54. In all hospitals there were 203 cesarean sections among 14,836 deliveries or 1 in 73, and for the entire City 203 sections in 33,988 births or 1 in 167.

TABLE I

HOSPITALS	CASES	SECTIONS	INCIDENCE
Jefferson Clinic	20	2	1 in 10
Deaconess	372	4	1 in 93
Delray	204	4	1 in 51
Highland Park	996	8	1 in 128
Booth Memorial	303	1	1 in 303
Lincoln	118	1	1 in 118
Women's	2153	47	1 in 45
Henry Ford	755	12	1 in 63
Providence	2236	11	1 in 203
Grace	834	16	1 in 52
Crittenden	1926	12	1 in 160
Harper	1535	48	1 in 32
Herman Kiefer	1734	7	1 in 247
St. Mary's	667	9	1 in 74
St. Joseph's	658	19	1 in 34
Marr	325	2	1 in 162
All Hospitals	14836	203	1 in 73
City total	33988	203	1 in 167

A marked variation in the incidence of section in different hospitals was noted varying from 1 in 10 to 1 in 247. This can be accounted for by a very few cesarean sections in a small number of deliveries in some hospitals and by the difference in the material applying for admission. Thus in two hospitals whose rates vary from 1 in 32 to 1 in 247, the work in the one is done almost entirely by obstetric specialists in the course of their private practice with many cases referred specifically for cesarean section, while the other hospital is a

\*Read before the Detroit Obstetrical and Gynecological Society, November 2, 1931.

teaching charity clinic drawing an average cross section of the City's obstetric practice.

*Indications.*—Seventy-three cesarean sections were done with contracted pelvis as the indication, which is the largest group. Thirty-four patients had had previous cesarean sections, the indication for which was permanent (i. e., contracted pelvis) in 20. The placenta previa group comprised 19 cases, 3 marginal, 6 lateral, and 10 central. These three groups comprise 126 cases or 62 per cent of all cases delivered abdominally.

TABLE II

Contracted pelvis	73	Long labor without progress	1
Previous cesarean section	34	Fractured pelvis	1
Placenta previa:	19	Amputation of cervix	1
Marginal	3	Rupture of cesarean scar at term	1
Lateral	6	Early rupture of membranes with	
Central	10	impending infection	1
Chronic myocarditis	9	Uterine inertia	1
Eclampsia	9	Ventral hernia	1
Disproportion	7	Procidentia	1
Fibroma of uterus	7	Pulmonary tuberculosis (with	
Abruptio placentae	6	sterilization)	1
Contracted pelvis (?)	5	Ununited fracture upper third	
(No measurements)		femur	1
Nephritic toxemia	4	Acute hemorrhagic nephritis	1
Elderly primiparae	4	Carcinoma of cervix	1
Preeclampsia	3	Echinococcus cyst of pelvis	1
Ankylosis of hip	3	Doubtful	4
Transverse	2		
Ovarian cyst	1		203

There were only four cases in which the information in the records left doubt as to the indication. This indicates a marked improvement in the keeping of current records in comparison with those of five years ago. On the other hand 5 cases in which the indication was "contracted pelvis" did not show pelvic measurements in the charts to warrant such diagnosis.

The group of eclamptics comprise 9 cases or 4.4 per cent. In my opinion eclampsia is no less frequent in Detroit now than five years ago, consequently there were far fewer sections done for this indication in 1930, as Welz reported 16.8 per cent done for eclampsia in 1925. Three sections were reported as being indicated by preeclampsia and 4 for fulminating nephritic toxemia. This in my opinion is not a surprisingly high number when we consider that many obstetricians think this indication valid.

Among the unusual indications, and one which I do not recall having seen reported in the American literature is an echinococcus cyst blocking the pelvic inlet. This was evidently a daughter cyst from the liver dropping downward and continuing to grow. Cysts of this character are not unusual in the South American countries and in Australia but are extremely rare in the United States.

"Premature rupture of the membranes with impending infection" was given as the indication in the case of a para iii at eight and one-half months in labor twenty-four hours. A low cervical operation was done and both mother and child were discharged on the twelfth day without complication. To this indication I cannot subscribe.

Early (Group I) carcinoma of the cervix was fortunately proved by biopsy late in pregnancy in one case and the patient delivered by section followed by wide panhysterectomy and removal of a vaginal cuff. Both mother and child survived without complication.

"Elderly primipara" accounts for 4 abdominal sections. This indication has always appeared to me as a rather doubtful one, although I must confess to having used it when there was an extraordinary demand for a living child and labor promised to be precarious for the infant. In a city of a million and a half population, it cannot be thought unusual that 4 cases should be sectional for this reason.

That pregnancy complicated by heart disease in the majority of cases is productive of no untoward sequelae is well known. Labor is often surprisingly easy and rapid. The prognosis of the cardiologist often is overshadowed by his unfamiliarity with the course of normal pregnancy, his outlook likely to be unfavorable "on general principles." Cesarean section seems to him to be the best advice for delivery at term in order to relieve the mother of "undue strain." His judgment, however, is not always vindicated by the course of events and many cases can safely be delivered from below with attention to detail and relief in the second stage. Nine cases in this series were sectioned for chronic myocarditis, all with good results.

*Maternal Mortality.*—There were nine maternal deaths from all causes among the 203 abdominal cesarean sections, a rate of 4.43 per cent. If correction is made for two deaths (4 and 9, Table III) the rate is 3.44 per cent. Of these one occurred in a patient with a psychosis who jumped from the window of her room, and died of shock. The other was the outcome of diabetes on the nineteenth day postpartum and could in no way be attributed to operation.

Compared with a 13 per cent maternal mortality for the City of Detroit reported by Welz for the year 1925 this shows a gratifying reduction. Five institutions in the City cared for more than 1,000 cases for the year 1930. In all 9,584 women were delivered and 125 sections done. 1 in 76. Three deaths occurred, a rate of 2.4 per cent. If corrected as above 1.6 per cent.

In ten hospitals 104 sections were done without maternal mortality.

It is interesting and instructive to note that all but one death in this series occurred after classical cesarean section.

In 105 cases the classical operation was done with 8 deaths, 7.61 per cent. If the correction is made as noted above, the rate is 5.71 per cent.

Among 87 low cervical operations there was no mortality. Eleven Porro operations were done with one death, a rate of 9 per cent. In 1925, as reported by Welz, 7.1 per cent of the total sections done in Detroit were low cervical. For 1930, 87 low cervical sections were done, 42.8 per cent. Slowly, all too slowly, we are learning the advantages of this type of operation in the conservation of maternal life.

TABLE III. MATERNAL MORTALITY

TYPE OF OPERATION	INDICATION	IN LABOR-HOURS	VAG. EXAM.	MEMBRANES	CAUSE OF DEATH
1 Porro	Fibroid blocking outlet	24	0	Intact	Peritonitis
2 Classical	Contracted pelvis	72	0	Ruptured 24 hr.	Peritonitis
3 Classical	Placenta previa centralis	0	0	Intact	Shock Hemorrhage
4 Classical	Eclampsia	0	0	Intact	Diabetes
5 Classical	Contracted pelvis	16	Attempt at forceps at home	Ruptured	Peritonitis Pneumonia
6 Classical	Placenta previa, meningitis	0	0	Intact	Shock Hemorrhage
7 Classical	Transverse	11¾	1	Ruptured 6 hr.	Peritonitis
8 Classical	Tuberculosis, right hip	0	0	Intact	Peritonitis
9 Classical	Placenta previa centralis	0	0	Intact	Psychosis death after jump from window

TABLE IV. STATISTICS OF THE LARGER HOSPITALS IN DETROIT

	CASES	SECTIONS	DEATHS
Women's	2153	47	1
Providence	2236	11	2
Crittenden	1926	12	0
Harper	1535	48	0
Herman Kiefer	1734	7	0
All Hospitals	9584	125	3

TABLE V

TYPE OF OPERATION		MATERNAL MORTALITY		
	CASES	DEATHS	PER CENT	CORRECTED
Classical	105	8	7.61	5.71
Low cervical	87	0	0	0
Porro	11	1	9	9

A more minute analysis of the maternal deaths (Table III) with reference to the case histories shows that in three instances (1, 2, 5) mortality could possibly have been averted by a different management of the cases in question. In Case 1 earlier operation was indicated. A classical section after seventy-two hours of labor and twenty-four hours after rupture of the membranes (Case 2) should not be considered. Classical section after attempted forceps delivery at home requires no comment (Case 5).

Three deaths occurred in the placenta previa group. As there were 19 cases the gross mortality rate was 15.8 per cent; corrected (Case 9, Table III) 10.5 per cent. Compared with the results recently reported by individual operations this rate is high. It will be noted in each instance that death was the result of shock and hemorrhage. Undoubtedly better results can be obtained if more careful attention is given to the condition of the patients with placenta previa *before* operation. Generous blood transfusion will prove a life saving measure in many cases. Care also should be taken, I believe, in making cesarean section the operation of choice with labor well advanced, as the use of the hydrostatic bag, or even tamponade of the cervix by pulling down one leg can many times be done with minimum loss of time, to the great advantage of the mother, even at the possible expense of the child.

Cesarean section was done for 9 cases of eclampsia, 3 of preeclampsia, and 4 of nephritic toxemia. One death occurred among the eclamptics, a diabetic who died nineteen days postpartum of this complication. There were no other deaths among the toxemias, a gross rate of 6.2 per cent. A rate corrected as indicated would give 0.0 per cent. Eleven deaths were reported by Welz in 1925, after abdominal cesarean section for eclampsia. In 1930 not only were far fewer eclamptics sectioned but the results in the patients operated upon were better.

*Fetal Mortality.*—There were 26 fetal deaths among the 203 sections, 12.8 per cent. Thompson in an analysis of cesarean section in Los Angeles from 1923 to 1928, reports a mortality of 7.9 per cent and with him I can agree that "cesarean section under ordinary circumstances should result in living babies, and the high figure noted needs more explanation than I can find."

TABLE VI. FETAL DEATHS 26, 12.8 PER CENT (CORRECTED 6.4 PER CENT)

Stillborn	10
Hydrocephalus	2
Cerebral hemorrhage	2
Severe toxemia	1
Prematurity	5
Asphyxia	1
Fetal atelectasis	1
Acute bilateral nephritis, eighth day	1
Congenital absence of both ureters and kidneys	1
Cause not given	2

Of the stillbirths 4 occurred in cases of abruptio placentae and 2 in placenta previa. Of 5 cases of prematurity, 2 occurred with placenta previa. Two cases of hydrocephalus suggest the more frequent use of x-ray before resorting to abdominal section. This fetal death rate shows no improvement over that reported by Welz for 1925. Even if 2 hydrocephalics, 5 prematures, 1 acute bilateral nephritis, 1 congenital absence of both kidneys and ureters, 4 abruptio placentae (Table V) in which the outcome would have been the same had delivery occurred normally from below are excluded, the rate is 6.4 per cent.

#### COMMENT

In considering the indications for cesarean section, it is gratifying to note the tendency to conservatism in the toxemias with convulsions. This tendency has been followed by a satisfactory reduction in the operative mortality.

The question of the treatment of placenta previa is still a debatable one in the minds of many obstetricians. That excellent results can be obtained by section in these cases is vouched for by many operators. Greenhill reports 44 cases without maternal mortality and states that his mortality by the so-called conservative methods is 3.9 per cent. His experience is confirmed by that of many others. On the other hand Williams says: "Thus far, very few cesarean sections have been done in our service for placenta previa and, as the results following the employment of the balloon have been reasonably satisfactory, I do not anticipate extending greatly the employment of section."

The death rate reported, herewith, is 10.5 per cent for placenta previa treated by section. This rate is too high and our attention in the future should be directed toward the lowering of the mortality in this group. Bill deserves much credit for having demonstrated the excellent results of combating shock and hemorrhages in these cases, with a reduction of his mortality rate from 11.1 per cent to 1.78 per cent. While a rate of 10.5 per cent is discouraging, we believe that this can be reduced and that we should not compare the worst results in the treatment of placenta previa by cesarean section with the best results achieved by the conservative treatment. It is also to be remembered that not all cases can be successfully treated by any one method, and probably the adoption of a "middle ground" course of procedure between section and more conservative measures will ultimately give the best results in the hands of most operators. In my opinion individualization of each case with the adoption of treatment apparently best suited will give the best results for the mother in placenta previa.

The group of cases in which contracted pelvis was the indication requires no particular comment. In the large majority of instances the case histories contained adequate pelvic measurements and reasonable test of labor was given in borderline pelvises.

Five of eleven Porro operations were done in one hospital, which admits a large number of neglected and poorly managed cases. There were no deaths in this series.

#### CONCLUSIONS

1. The maternal death rate from cesarean section in Detroit has dropped from 13 per cent in 1925 to 4.43 per cent (corrected 3.44 per cent) in 1930.

2. The fetal mortality rate does not show the same marked improvement. The rate for 1925 was 11 per cent, that for 1930, 12.8 per cent (corrected 6.4 per cent).

3. The indications for cesarean section seem to be well known, although in the city at large, there can be no doubt that cases occur which if properly evaluated late in pregnancy or early in labor would be sectioned rather than subjected to disastrous attempts at delivery from below.

4. The contraindications are not so well known or at least not so well observed, with frequent unfortunate results.

5. The low cervical cesarean section should replace the classical operation as the operation of choice in the majority of cases.

6. While the low cervical section permits a real test of labor to be given women with borderline contracted pelvises, and is permissible on occasion after rupture of the membranes, and possibly, at times, in potentially infected cases where a living child is greatly to be desired, yet it must be remembered that it should not compete with the Porro operation or with craniotomy.

7. The reduced maternal death rate can be attributed, in part, to the comparative infrequency of cesarean section for eclampsia.

8. Case records show improvement.

Appreciation is expressed to Dr. David Davidow, Resident Obstetrician at Herman Kiefer Hospital for invaluable aid in the collection of data.

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DAVID WHITNEY BUILDING.

# AN ANALYSIS OF ONE THOUSAND OBSTETRIC CASE HISTORIES\*

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IF ONE is to practice good obstetrics, three things are to be accomplished: First, the patient should be guided through her pregnancy by careful antenatal care, so that she arrives at full term in the best of physical condition; second, she should be delivered, if possible, of a living child with the minimum amount of suffering and traumatism to both herself and the newborn infant; and third, her care during the puerperal period should be such as to enable her to resume, as quickly as possible, her former place in that strata of society from whence she came.

\* \* \* \*

Knowing that statistics never lie, although statisticians have been known to prevaricate, I have selected for presentation an analysis of my last one thousand consecutive private obstetric case histories. This subject was selected, not so much to offer to you a volume of statistics, as to discuss the treatment of various complications arising in a series such as this, and to suggest that fair obstetrics might be practiced without having any unusual dogmatic rules.

\* \* \* \*

May I also say in this foreword, that I am irrevocably in favor of teaching undergraduate students the most conservative type of obstetrics, call it as you will, masterful inactivity, aseptic watchful waiting, or the Garden of Eden method. I believe however, that if a man is at all competent and is delivering all of his patients in a well equipped modern maternity hospital, with trained assistants and skilled anesthetists, it is justifiable to relieve a woman as much as possible of the pains of labor providing no extra traumatism to either mother or child occurs.

The patients from whose histories I have gathered these statistics have all been treated by myself, although a few have been delivered by my associates while absent from the city, and include all patients seen in consultation who have been admitted to my private service for delivery.

## MATERNAL DEATHS

There occurred in this series of 1000 pregnant women, 3 maternal deaths.

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\*Read by invitation at a meeting of the New York Obstetrical Society, November 10, 1931.

For lack of space it is not possible to publish this paper in full. The complete paper may be had in the author's reprints.



The first patient died of subacute bacterial endocarditis when three and one-half months pregnant. She was seen for the first time three weeks before her death, at which time the diagnosis was suspected. She was immediately hospitalized when it was found she had a positive *Streptococcus viridans* infection and that death was inevitable. This occurred two weeks later.

The second death occurred in a woman seven and one-half months pregnant. She had been seen for the first time two weeks previously and no abnormalities were noted. She was found dead in her home and although the deputy coroner and family insisted she died from toxemia of pregnancy which I had overlooked, supposedly, on my primary examination, it was quite natural that I would insist upon an autopsy being performed. The autopsy revealed the stomach to be filled with a rather clear fluid, formerly sold as gin, but in this particular instance consisted mostly of wood alcohol.

The third death followed cesarean section in a patient seen for the first time in labor. She was a primipara, forty years old, who had been perfectly well during her entire pregnancy. I was asked to see her after she had been in labor actively for ten hours. There was no engagement of the presenting part, there was no effacement of the cervix, and there was no dilatation. She had a slightly contracted pelvis. There had been no vaginal examinations made and there was no manipulation or attempt at delivery performed. Cesarean section was decided upon and she was sent to the hospital. Before being taken to the operating room she prophesied that she was going to die and continued to prophesy such many times each day following operation. In spite of medical consultation and sedatives, all efforts to change her opinion were of no avail and her prophecy was fulfilled on the fifth day. Complete autopsy showed no visible pathology.

#### ABORTIONS AND PREMATURE LABOR

Of the 1000 women who were seen, examined and found pregnant, 71 did not go through to full term. For purposes of discussion, any child born during or after the eighth month is included in a separate group considered to be at or near full term. No patient was included in this series who was seen for the first time during an abortion or miscarriage, nor does it include any patient who was seen for diagnosis of pregnancy and who expressed an opinion that she would have a criminal abortion done, or any patient referred by other physicians for diagnosis only.

Of the 71 women who were not delivered of full-term children, 47 aborted before four and one-half months. In looking for the causative factor in these 47 patients, I have been impressed by two things: first, the absence of syphilis, and secondly, the frequency of the history of sexual intercourse preceding within twenty-four hours the onset of the first symptom. In this group of 47 who aborted during the early months of gestation, many suspected causes were noted, but the vast majority were put down as unknown. It is interesting to note that 12 of these same patients' names appear later in this series as being delivered of full-term children.

\* \* \* \*

The rest of these patients who gave birth to stillborn babies between four and one-half and eight months, were as follows:

Polyhydramnios with monstrosity	3 cases
Influenzal pneumonia	1 case
Hydatidiform mole	1 case
Placental separation due to disease of the placenta	1 case
Preeclamptic toxemia	3 cases
Cause unknown after careful examination of placenta and autopsy of the child	5 cases

In addition, pregnancy was terminated because of the health of the mother in 10 patients:

- 1 being done for pernicious anemia
- 4 for cardiac disease
- 1 in chronic nephritis, and
- 4 cases of pernicious nausea.

These 4 cases of pernicious nausea were all exceedingly severe and were all seen late in the disease. It is interesting to note that pregnancy has not been terminated because of pernicious nausea and vomiting in the last two and a half years.

#### TOXEMIA AND OTHER COMPLICATIONS OF PREGNANCY

In addition to the cases listed under abortion and premature labor, toxemia occurred severely enough in the following patients to warrant admission to the hospital for treatment: 9 patients had pernicious vomiting, all of whom responded to treatment and carried their babies to full term; 11 had preeclamptic toxemia, 9 of whom were delivered of living children at or near full term, 2 had stillborn babies during the last month; 3 patients developed eclampsia.

\* \* \* \*

Preeclamptic toxemia is treated by rest, sedatives, isolation, elimination, glucose intravenously, and low protein salt-free diet. If there is no improvement, or the condition becomes worse, termination of the pregnancy is indicated.

The method of termination depends upon the individual case. Either induction of labor or if in a primipara with severe toxemia at or near term with no engagement of the presenting part and an elongated, thick cervix, hysterotomy under local anesthesia. When convulsive toxemia occurs, the modified Stroganoff treatment is instituted, morphine, colonic irrigation, gastric lavage, purgation, glucose or magnesium sulphate intravenously, and sometimes venesection and hot dry packs. In these patients, I believe it is advisable to forget for the time being, that they are pregnant, and devote one's effort entirely to the treatment of the toxemia. Most of these patients will go into labor shortly after the onset of the convulsion. When labor has progressed to the point where it can be terminated without using accouchement force, the patient is de-

livered. When an eclamptic improves to such an extent that the convulsions cease without the patient going into labor, I believe it should be induced during that period of quiet which usually precedes a storm more violent than the first.

I can only condemn the routine use of cesarean section in eclampsia. The only indication for performing this operation being some other condition associated with the toxemia which is an indication for abdominal delivery and then only if the patient has had twenty-four hours of active eliminative treatment. I have, on a few occasions, sectioned patients who were brought in with convulsions and who at the end of twenty-four hours' active treatment showed no signs of improvement. These patients were all primiparous individuals with the presenting part unengaged, a cervix which was not dilatable, and a living baby in utero.

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I believe the above statement is sufficient evidence to prove that I am a firm believer in cesarean section for central placenta previa. Lateral, marginal or low attached placentas should be treated according to each individual patient, taking into consideration the parity of the patient, the amount of dilatation, the viability of the child and the general condition of the patient. There were no cases of marked placental separation of a normally implanted placenta, except in those cases which were classified under abortions and premature labor before the eighth month.

#### PARITY, PRESENTATIONS, AND METHODS OF DELIVERY

Subtracting the 71 cases who aborted or had premature labor before the eighth month, together with the two women who died without being delivered, leaves 927 women who were delivered during or after the eighth month of gestation.

Of these 927 women, 573 were primigravida and 354 were multigravida. There occurred in this group of 927 patients, 8 sets of twins, making 935 babies actually delivered. It has been the custom in all twin pregnancies of delivering the second child immediately after the first has been born, without allowing the patient out of the anesthesia, because of the possibility of a small baby developing a compound presentation, or the cord prolapsing.

Of the presentations of these 935 children, there was one face presentation, one transverse lie with a prolapsed arm, 30 babies presented by the breech, and all others were vertex. The one face presentation was delivered by internal podalic version, as was the one patient with the transverse lie and prolapsed arm. The 30 babies presenting by the breech were all extracted when the dilatation of the cervix was complete.

The question as to whether or not a breech presentation should be allowed to go on to spontaneous delivery is one which has been argued back and forth for some time. In the majority of breech presentations,

particularly those occurring in primiparous individuals, the labors are very much longer and very much more severe than the ordinary head-first presentation. It is therefore natural that more of these patients should suffer from exhaustion before the labor is terminated, and furthermore, that delivery of a spontaneous breech is not as easily accomplished under obstetric analgesia as is a spontaneous head presentation.

As all of these cases occurred in private practice, as all were delivered in a hospital where trained assistants and equipment was at hand, a great deal of the traumatism and suffering of the mother did not occur. I believe however, that unless one is so situated that good anesthesia and proper help is available, interference with breech presentation invariably leads to a high fetal mortality.

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In this series of 30 breech presentations extracted when the cervix was completely dilated, there occurred no maternal mortality and all babies survived.

The occiput in a posterior position was diagnosed in this group of vertex presentations 204 times. Although most textbooks make the statement that a very high percentage of these cases will rotate anteriorly if allowed to go long enough, it has not been my experience in private practice. Patients presenting this abnormal rotation of the head have caused me more anxiety and made it necessary for interference more frequently than in any other type of obstetric case handled. To say that all posterior positions should be treated in any one way, I believe to be wrong. Each individual case should be treated according to the exact condition present. If I were to be asked the question, "What is the treatment of the posterior rotation of the occiput?" I would make the following statement: If the patient were seen with complete effacement of the cervix and at least three-quarters dilatation, the membranes unruptured, the cervix dilatable, no disproportion between the pelvis and the child and the patient having had active labor for several hours, I would deliver her by internal podalic version. This may be a rather radical form of treatment but we have found in these selected cases, many hours of labor have been saved without any undue traumatism to either the mother or the child. If the patient is seen after the membranes rupture, the cervix only being partially dilated, waiting with the patient relieved by either modified twilight sleep or rectal ether analgesia is the choice of treatment.

If for some reason, such as, exhaustion on the part of the mother or undue pressure upon the child, interference is indicated with the occiput still posterior; the following procedure is carried out: The patient is completely anesthetized, placed in lithotomy position, with the bowels and bladder emptied and the usual external preparation. Careful vaginal examination is then made to decide the best method of procedure.

If manual rotation of the head is possible, it is rotated in anterior position and forceps applied; if it is found to be impossible to rotate the head manually, forceps are applied and either according to the method of Bill, the head is rotated in the plane of the pelvis in which it is arrested, or is pulled down to the pelvic floor in a posterior position when a Scanzoni maneuver is done. Most of these cases, we find, can be rotated almost to the transverse position by the hand and the rotation completed by the forceps.

The instrument used is usually the Bill modification of the Tucker-McLane forceps. It is only occasionally that rotation of the head by instruments is impossible when the head is delivered with the occiput still posterior. It is advisable not to do this as injury to both mother and child are more likely to occur. Occasionally, even though the membranes be ruptured, it seems best to deliver these cases by internal podalic version rather than to do a difficult extraction with forceps.

Of the 935 babies delivered, 303 were born spontaneously. I use the word spontaneous in preference to normal delivery, because a large number of women give birth to their children without aid from the attending physician whose labor I would not consider normal. For example, a woman may give birth to a child spontaneously at the end of sixty hours labor, but I would not consider a labor normal when the patient had been in labor that long. Practically all patients delivered had relief from the first stage labor pains by either morphine and scopolamine, or by rectal ether analgesia. All spontaneous cases were delivered under light ether anesthesia. No episiotomies were done without an anesthetic, and if any laceration occurred during a spontaneous delivery, anesthesia was given to the patient before the repair was done.

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#### FORCEPS

Four hundred twenty-six of these children were delivered instrumentally. I have divided them into two classes of cases: First, those patients where the head was on the pelvic floor with the occiput rotating anteriorly and where the only indication for the use of instruments was to relieve the patient of the second stage labor pains. In this group there were 325 deliveries. The other 101 patients delivered by forceps were cases in which interference was necessary due to either exhaustion on the part of the mother, embarrassment of the fetal heart, or some failure in the mechanism of the rotation of the head. A very large number in the second group consisted of cases which could not be classified as posterior rotations of the occiput, but which I would prefer to classify as delayed or deficient rotation where good cephalic application could be made with the occiput anterior to the transverse median line of the pelvis. It might be stated that these 325 women delivered mostly to save them the excruciating pains of the second stage of labor, would have delivered them-

selves if allowed to go on for a period of a few hours. In this group there were no traumatisms either to the child or to the mother, and in most of this series the patients were primiparous individuals where the pelvic floor and perineum were fairly tight and where episiotomy was thought advisable.

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For the last two or three years I have used exclusively on these outlet or low cases, the Tucker-McLane forceps with the Bill axis-traction modification. I do not feel that this is an instrument that can be used where a moderate or a great amount of traction is necessary, but for rotating the head and for delivery when the head is well down on the pelvic floor. It has been my impression that less sulcus lacerations occur and less compression is made on the child's head with this instrument than with any of the outlet forceps that I have ever tried. The obstetric forceps for a good many years have been condemned for some reason or another. Properly applied forceps with steady traction instead of irregular jerky pulling, I believe very seldom causes cerebral hemorrhage, and I also believe that to know when to put the forceps on rather than as to how to put them on is of paramount importance. In other words, if I can teach my resident not to apply forceps to the head of the child before it is out of the cervix and before rotation has occurred, I feel I have saved many children in the future.

In the group of 101 patients where interference was absolutely necessary there were several very difficult deliveries. All in this group would come under the classification of mid forceps or high mid forceps. It has been a long time since I have applied forceps above the pelvic brim and believe that to do so certainly invites disaster either to the mother or the child. The advocates of the Kielland forceps may be perfectly right in the use of this instrument above the brim of the pelvis, but after attempting on several occasions to use this instrument, I have discarded it entirely. If the head is so high as to be at the brim or out of the pelvis, I would much prefer delivering the patient by internal podalic version. The Barton forceps and various other makes have all been tried as they have been placed on the market. At the present time I would say that Bill's modification of the Tucker-McLane forceps, one set of axis-traction forceps either DeWee's or Piper, and the after-coming-head forceps of Piper, are all that are necessary. I would like very much at this time to endorse the use of the Piper after-coming-head forceps in the use of either breech extraction or extraction following podalic version. The 30 breech cases which are reported in this series all had after-coming-head forceps applied to them, and at the present time their application to the head of the child is done routinely. I am absolutely certain that this instrument has saved several babies in difficult extraction which would otherwise have been lost.

## VERSION

Seventy-five babies were delivered by internal or combined, or properly called Potter method; although I do not agree with Doctor Potter in his indications for delivering the majority of children by this method, I believe there is no question that what he has taught us in doing version and extracting the child is far superior to the old method of doing so, and in these 75 cases of version, his technic has been followed out as closely as possible.

The indications in these cases were mostly posterior positions with unruptured membranes or high arrest of the head with failing contractions of the uterus in multiparae where the bag of waters was still intact. There need be no doubt, I believe, in the fact that the operation of version done before the rupture of the membranes is a much simpler procedure than when done in a dry uterus. Piper has suggested recently the injection of green soap through a rectal tube and syringe into the uterus in those cases where version is done after the membranes rupture. My experience with this method has been very slight, but I believe that it aids materially in the ease with which the child can be turned. Version also has been much criticized by many men, and here again I feel very strongly that to know when to do the version is more important than to know how. The reason that version has been condemned so vigorously has possibly been due to the fact that some men have used it as an operation to be done as a last resort after forceps have failed, rather than as an operation to be done at the time of election. I believe also, that there are more cases of cerebral hemorrhage in infants delivered after version and spontaneous labor than by delivery with the obstetric forceps.

## CESAREAN SECTION

One hundred and one patients in this series were delivered by abdominal section. This of course, is an especially high percentage of patients to be delivered by this method out of 927 confinements. However, a careful scrutiny of these records show that 69 of the 101 patients in this group were seen for the first time during labor, at the onset of labor, or were referred because the family physician noted abnormalities which would necessitate abdominal delivery.

The indications for delivering these patients abdominally were as follows: 49 patients had disproportion. I use the word disproportion instead of contracted pelvis because in some of these individuals the size of the pelvis was ample but the relative size of the child was not. For example, one patient weighing 269 pounds, who had an external conjugate of 20 cm., primipara, thirty-six years old, was delivered of a child weighing 11 pounds and 8 ounces; 6 patients had central placenta previa; 4 primiparae who had preeclamptic toxemia at or near full term were delivered by abdominal section under local anesthesia as a matter of choice rather than having labor induced; 5 patients who had serious

cardiac damage, in other words who were classified as very poor risks for labor, were delivered by abdominal section under local anesthesia; 8 patients beyond forty years of age who, after a test of labor showed no ability to dilate the cervix, were operated upon. One of these patients was fifty-two years old and had had no children for twenty-one years. Eighteen patients had had previous cesarean section; one patient was delivered by the abdominal method because of a brain tumor which was growing rather rapidly, and it was thought impossible to allow her to go into labor; there was one case of a monstrosity, an acardiacus cephalus, the second of a pair of twins, which has been reported in the literature about a year ago; one patient had had an extensive plastic operation with ventral fixation of the uterus without sterilization and which caused sufficient dystocia that abdominal delivery was necessary; 2 patients with uterine myoma obstructing the birth canal had cesarean sections and myomectomies performed; 4 patients because they had lost their first baby and because they had borderline pelvic measurements, elected to be delivered by abdominal section rather than to have a test of labor; one patient with marked epilepsy was delivered by abdominal section for sterilization; one patient having moderate cardiac disease and upon whom medical consultation advised sterilization, was delivered by abdominal section and sterilized.

#### MORTALITY

Of these 101 patients delivered abdominally, one patient died as reported previously in this paper. As I look back upon this one mortality I can see no way in which this could be obviated. I have in the past sent patients back from the operating room who have informed me just previous to taking the anesthetic, that they would not survive the operation. It is one thing in which I am very superstitious, but in this case it was absolutely necessary that this woman be operated upon, and as I recall this patient, the only thing that she said to me before operation and for five days following operation, was that she was going to die. What this peculiar mental complex might be I do not know but there certainly was no pathology shown at autopsy which could account for her death. There were 102 babies delivered from these 101 women. One case being a twin pregnancy complicated by uterine myoma. Of these 102 babies, the following did not survive: The child born of the patient with the brain tumor was just over the eighth month, was born alive and died of prematurity one week later. The monstrosity had no head and no heart and therefore it could not survive. In the one twin pregnancy delivered by abdominal section, the smaller of the two babies succumbed on the fourth day from atelectasis of the lung. One child born of a mother who had serious cardiac damage died of cerebral hemorrhage. I have reported this case in detail previously but will state the salient facts here: this patient had not been in labor, the head had not



been in the pelvis, she was delivered by abdominal section under local anesthesia, the child was not dropped, and developed signs of intracranial hemorrhage within two hours after delivery. It died forty-eight hours later. Complete section of the brain showed that the entire vascular system was made up of a basement membrane upon which was placed one layer of endothelial cells. This is one case in which it could not be possible for any traumatism to have occurred either from the force of labor pains or in the delivery itself. One other child delivered by section from a patient suffering from serious preeclamptic toxemia died on the fourth day. This child was premature.

#### TYPES OF OPERATION DONE

Eight of these patients had performed upon them the low or cervical section. All the others had the so-called high operation. With the advent of the low cesarean operation many men have discarded the simple incision of the uterus in all patients delivered by abdominal section. Although at the present time any patient whose membranes have ruptured for any length of time or who has had an attempted delivery from below, I believe should unquestionably have a flap operation done, but unless there has been some manipulation through the vagina, I cannot feel that the ordinary cesarean section is not suitable. By the ordinary cesarean section however, as we have done for several years, I do not mean an incision in the fundus of the uterus.

The technic that we have employed for several years has been to make the incision low down in the anterior wall of the uterus and I believe that the importance of the entire operation lies in the closing of the uterine incision. We use mattress sutures in the myometrium, 2 continuous layers of catgut in the myometrium also, and the peritoneal layer closed by a Cushing stitch or by a continuous suture which inverts the peritoneal layer and completely covers over the uterine scar. This method of closure done carefully, has been exceedingly satisfactory, so that our theory has been—Why do a technically more difficult operation when results are so satisfactory? That the low cervical operation has resulted in the saving of many women is not questioned. For example, one ward patient recently who had had 28 vaginal examinations on the outside, with 3 anesthetics and 3 attempts at forceps delivery by 3 different men, having a baby weighing 10 pounds and 9 ounces, and an extremely bad risk for a celiohysterectomy, made a very nice recovery after this operation was done. I have no objection to the operation except that I feel it is more difficult to do and that the patient usually has more blood loss. My only reason for not doing it routinely is because where no manipulation has been performed, I can see no reason for giving up an operation which has proved eminently satisfactory. We hear very frequently, from one source or another, that there are too many cesarean operations being done. In retrospect of these 101 patients operated upon, there are none that I was sorry that I had performed cesarean section upon.

## FETAL MORTALITY

Of the 935 children delivered during or after the eighth month of pregnancy, 376 were females and 559 males. Of these 935 children delivered, 29 babies did not survive.

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Of these 29 infant deaths there probably were at least 2 or 3 preventable. In 2 cases that were delivered by version the children were alive when the patient was anesthetized for delivery. Both babies were large, and a version was performed in both cases with extreme difficulty. If the proper size of the child had been estimated, version would probably not have been done.

## SUMMARY AND CONCLUSIONS

This is a report of 1000 private obstetric patients. All patients who delivered before the eighth month are classified under abortion and premature labor. There were 71 in this group. In addition to these patients, 20 patients had toxemia severe enough to necessitate hospital care; 6 patients had central placenta previa. The pregnancy was terminated in 10 cases because of disease of the mother. Nine hundred twenty-seven women were delivered during or after the eighth month of gestation, 573 were primigravidae, and 354 were multigravidae. In this group of 927 patients there were 8 sets of twins making 935 babies actually delivered. There was one face presentation; one transverse lie; 30 babies presented by the breech, and all others were vertex. Of the 935 babies delivered, 303 were born spontaneously, 426 were delivered instrumentally, 75 were delivered by version and 101 by cesarean section. There were 3 maternal deaths, 2 during pregnancy and one following delivery.

## CONCLUSIONS

As previously stated in this paper, I did not select this topic to quote a lot of statistics, but rather to discuss various methods of treatment of the normal and complicated case of pregnancy. The main point which I would like to stress is the necessity of studying each individual patient no matter what the complication is, before deciding on the plan of treatment. We all seem to have a tendency to give up older methods when new ones are promulgated by some leader in the profession. But is it not more practical not to become too enthusiastic about any one certain procedure because in any one individual's hands it seems to be the ideal method? In other words, this is not a criticism of Potter's version, prophylactic forceps of DeLee or any of the low cesarean operations, but rather a plea to hold one's enthusiasm down the center of the road and use those methods which seem to be the best under one's own surroundings and be able to appreciate one's lack of ability to do things which have proved successful in someone else's hands.

I have been very much impressed during my few years in the practice

of this specialty, with which the pendulum seems to swing from one side far over to the other, and I feel very strongly that to keep the pendulum more in the center is going to be of greater aid to women during pregnancy and childbirth and is also going to help place the specialty of obstetrics upon that high plane to which I think it rightfully belongs.

May I again reiterate that to teach undergraduate students who are going out into the practice of medicine in small communities in the country and who are going to practice obstetrics both in the home and in poorly equipped hospitals should be the most conservative type of teaching. No one can say that to allow a woman to go on in labor does more than to cause her to suffer longer than would seem necessary under different circumstances, as we are all aware of the fact that if most patients are allowed to go on in labor they will eventually deliver themselves. However, in this present day and age, where one is practicing obstetrics in a modern maternity hospital, with capable assistants and competent anesthetists, much can be done to relieve women of the pains of labor without causing any undue traumatism to either the mother or child. If one is so situated, I believe it is perfectly justifiable to interfere during the progress of labor much more frequently than we would advise being done by the general practitioner of medicine under different surroundings.

And finally, may I suggest to you that the three problems which confront the obstetrician today and in which a great deal of good can be accomplished, are: first, further research into the question of toxemia; second, the justifiable relief of pain during the actual act of childbirth; and third, more extensive and active postnatal care of each individual patient.

1731 PINE STREET.

(For discussion, see page 146.)

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**Bacialli: The Passage of Tuberculous Substances Through the Placenta.** Riv. Ital. Ginec. 9: No. 2, 1929.

The author reports the results of his experiments on guinea pigs with tuberculous filtrates.

Subcutaneous injections of filtered excreta in pregnant guinea pigs do not affect pregnancy or parturition or lactation, even though they produce the usual pathology in the mother animal. The offspring of such guinea pigs are born free from any pathologic changes. The offspring of these inoculated guinea pigs when inoculated in a similar way and with analogous material do not show neither increased nor lessened sensibility to such inoculations.

The experimental results of the author are identical with those of Arloing, Vaudremeyer, Durand, Valtis, Negre and Bouquet. He believes that these experiments place grave doubt on the existence of a tuberculous, filtrable virus and on the possibility of its passage through the placenta.

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## END-RESULTS AFTER EXCISION OF THE CERVIX INTERPRETED FROM PATHOLOGIC FINDINGS\*

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OPERATIVE measures for the relief of leucorrhea aim to remove the infected endocervical mucosa, from which the discharge originates. This paper tabulates the results obtained by conical excision of the cervix in 130 patients operated upon at the Long Island College Hospital, between February, 1927, and May, 1930. Only proved cases of inflammatory cervicitis, and those followed for at least one year are included in this study. Trichomoniasis was excluded in cases of vaginal discharge recurring after operation.

Viewed in the light of end-results, removal of the endocervix either by amputation, or the more conservative excision, has not proved entirely satisfactory. R. M. Rawls, in a series from the Woman's Hospital, in which the technic of Emmett was employed, reported 60.7 per cent cured, 31.1 per cent improved, 7.1 per cent unimproved and 1.1 per cent as aggravated following operation. H. B. Matthews, employing the Sturmdorf technic in a series of 70 cases, recorded 70 per cent cured, 22.8 per cent improved, and 7.2 per cent unimproved. In a follow-up group of 75 patients from the Bellevue Clinic, operated upon by the Sturmdorf technic, F. W. Sovak tabulates 88 per cent cured, 4.7 per cent improved, and 5.3 per cent as unimproved. In this series of 130 cases, the Sturmdorf technic was used, although in the older patients and in those requiring extensive plastic operation, removal of the cervix was more radical. Catgut replaced silkworm for the inversion suture in restoration of the portio. Preoperative preparation consisted of thorough application of one-half strength tincture of iodine to the vulva, vagina, and cervix. Where curettage was performed, a quarter-inch iodine pack was placed in the cervical canal and retained during extirpation. In cases of prolapse, douches of bicarbonate of soda and boro-glyceride tamponade were employed for several days prior to operation. In this series of 130 cases, 103 or 79.2 per cent were cured, 23 or 17.7 per cent were improved, and 4 or 3.1 per cent received no benefit (Table I). In one of every five cases therefore the ultimate operative result was unsatisfactory. It is the purpose of this paper to analyze the causes of failure.

Broadly speaking, leucorrhea, recurring after cervical operation may be immediate or late. In the latter instance, a symptom-free interval of several months is present and vaginal discharge results from reinfection

\*Read by invitation at a meeting of the New York Obstetrical Society, November 10, 1931.

of a retained endocervical segment, if vaginal moniliasis and trichomoniasis are excluded. However, where leucorrhea continues from the time of operation, it may be the result of (1) operative infection in a retained healthy endocervical segment; or (2) retention of an inflamed endocervical segment, already infected prior to operation. Pathologic examination of the cervix and endometrium, where available, serve to determine these factors.

Our routine laboratory study of the excised cone, includes notation of the length, transverse and anteroposterior diameters, at the portio and apex; as well as thickness of the muscle segment. Lacerations and erosions are described. The excised cone is then slit laterally and the endocervical mucosa is exposed from apex to portio, permitting complete observation. Tissue blocks are then cut from the anterior and posterior walls, reaching from the portio to the apex, and including the endocervix with its segment of underlying muscle. Several slides are examined from each block. Serial section study is not attempted.

Pathologic changes observed in this group of 130 cervixes are essentially those recorded in the literature of cervicitis. Emphasis, however, must be placed on the observation, that endocervicitis is most frequently partial and limited to the lower segments of the endocervix, generally in the areas of laceration, ectropion and eversion. Inflammatory involvement of the muscle coat above the portio is rare and was demonstrable in only one case. Acute endocervicitis was present in only one specimen. Subacute or chronic endocervicitis or both was the usual finding. Subacute endocervicitis with or without erosion was encountered 48 times. It indicates infection confined to the mucosa, and is evidenced by small round cell exudate in the stroma. The glands are hypertrophied, and the constituent columnar cells intensively secreting. Adenomatous proliferation is common. Edema and congestion are present. In chronic endocervicitis, round cell exudate is less prominent, vascular congestion recedes and interstitial fibrosis appears. Antecedent hypertrophy and hyperplasia of the glands often persist. As the process reaches a more advanced healing phase, fibrosis is even more marked and glandular cysts frequently appear. If of sufficient size they encroach upon the muscle layer and bulge into the canal. Retention cysts result from pressure upon the gland outlets, by the proliferating stroma. Combination of subacute and chronic endocervicitis was noted in 81 specimens. Erosion of the portio is frequent and occurred in one-half of the cervixes. It indicates antecedent epidermoid desquamation due to infection and maceration. The resultant ulcer is soon covered by heterotopic endocervical epithelium, producing the clinical erosion or first healing phase. This was encountered six times. The columnar epithelium now lining the portio, may be confined to a solitary surface layer, or may be arranged in pseudopapillae, or true glands. The erosion is accordingly designated as simple, papillary, or follicular.

Secretion from this aberrant epithelium is intensive, contributing to the discharge. The stroma underlying the erosion is infiltrated with round cells. Congestion is present. With recession in inflammatory intensity, the second healing phase appears, and is evidenced by return of the surface epidermoid lining. This was noted in 56 cases. Regeneration proceeds from epidermoid cells at the sides of the erosion, and from islands of epidermoid cells which have escaped destruction in the initial stage of infection. In the third healing stage of the erosion, removal of the heterotopic columnar elements beneath the epidermoid lining is accomplished. This phase was encountered only three times. The underlying gland spaces are surrounded by nests of epidermoid cells arising by metaplasia from columnar epithelium, and also from the basal zone of the overlying epidermoid layer. The picture of precancerous cervix is thus produced. Ultimately, the gland lumina are compressed, the columnar epithelium destroyed, leaving an epidermoid column in communication with the surface which is later resorbed. Obliteration by direct growth of epidermoid cells into the lumina of the glands is also encountered. In the end stage, exudate is resorbed and fibrosis appears. As healing is not always complete, glands are occluded producing typical nabothian follicles at the portio.

Although pathologic diagnosis is important, surgical end-result, however, is more vitally concerned with (1) the degree of removal of the endocervix and (2) the degree of endocervical infection in the individual cone. In this series of 130 specimens, complete anatomical extirpation of the endocervix was accomplished only in one instance, the presence of endometrial glands at the apex of the cone indicating such accomplishment. Axiomatically, therefore, a segment of endocervical mucosa is retained above the level of transection after excision of the cervix. In young women, the low excision was frequently deliberate. In 57 cases, previous dilatation had obliterated all landmarks of the internal os, recognized at best with great difficulty, due to absence of a circular sphincter in this zone. Not only does examination of the excised cone prove inadequate excision of the endocervix, but determination of extent of infection in the endocervical cone indicates the physiologic status of the retained endocervical strip. From this viewpoint, (1) "a partially infected cone," (2) a "completely infected cone" group are differentiated. The partial form was arbitrarily divided into two subgroups. (A) "The low infection cone," in which the inflammatory zone does not extend above the lower third, and (B) "The intermediate infection cone," in which infection extends beyond the lower third but does not reach the apex, where healthy mucosa is retained. Since the mucosa at the apex of the excised cone is normal, the endocervix retained above the line of transection is normal. The second group or the "completely infected cone" displays inflammatory exudate extending from external os to apex. The excision may coincidentally remove the en-

tire inflammatory area leaving a normal endocervical segment in situ; or the excision may be incomplete with retention of a previously infected endocervical segment. In either cone type, if the retained endocervical segment is healthy, postoperative leucorrhea results from operative contamination and infection. The inversion suture is one offender. Operative measures as dilatation and curettage or radium insertion frequently performed with excision, afford even greater infective opportunities, for instruments are passed from an infected zone below to healthy endocervix above. In 16 cases of excision of "low infection cones" associated with curettage there were three failures, an incidence of 19 per cent (Table VI). Of three cases associated with radium insertion, there was one failure, an incidence of 33 per cent (Table VII). This contrasts strikingly with an incidence of three failures in 28 cases where these operative procedures were omitted (Table VIII). In the "intermediate infection cones" similar results obtain. There were 4 operative failures in 15 cases where dilatation and curettage was performed (Table VI) and 4 failures in 8 cases with radium insertion (Table VII). In striking contrast there was only one failure in the remaining 22 cases of this group in which these operative measures were omitted (Table VIII). It must be emphasized that in the radium group, the cervical pack necessary to retain the radium in situ causes edema of the mucosa in addition to introducing infection. Removal of the pack may also loosen the inverting suture, allowing retraction of the flap with exposure of the stump to vaginal bacteria.

In the "group of completely infected cones" where excision has removed the entire inflammatory area, retention of a healthy endocervical segment similarly allows operative infection. Here, too, curettage and radium insertion play important rôles. In 11 cases where dilatation and curettage were performed, there were five failures (Table VI). In 4 radium cases there were 2 failures (Table VII). Seven failures in a series of 15 cases contrast with an incidence of 4 failures in 23 remaining cases where such procedures were omitted (Table VIII). Late operative contamination may also occur. It is the result of vaginal pack employed for the control of postoperative bleeding, encountered in 5 patients of this series. Three were completely cured; one was improved, and one patient was unimproved. Both failures occurred in "completely infection cones" and are here appended (Table IV). The "complete infection cone group" as previously noted may also be associated with retention of an endocervical segment infected prior to operation. This in itself militates against operative cure. The exact frequency of this occurrence is difficult to establish but can be gaged if curettings are available. In absence of recent gestation of tuberculosis, inflammatory endometritis is an upward extension of endocervicitis. When endometritis, therefore, is associated with a "completely infected cone," the assumption is warranted that infection exists in the retained endocervical segment inter-

mediately located between the excised cone and the uterine cavity. In 15 of 38 cases in this group curettings were available. Seven showed the lesion of inflammatory endometritis with etiology as follows (Table V): One case presented an infected cervical polyp extending from the zone of the internal os; the second a submucous cervical fibroid with a patent canal and os. Four cases were associated with salpingitis as proved by operation indicating gonorrheal etiology in the coincidence of endocervicitis, endometritis and salpingitis, although no bacteriologic examination was made. In the seventh case the causative factor could not be explained. Infection of the retained endocervical segment appears certain in 6 of 38 "completely infected cones." Persistence of leucorrhea from this cause alone is evident. For although the incidence of curettage and radium insertion is lowest in this cone group (39.4 per cent) yet end-results are poorest for in 38 cases only 71.1 per cent were cured, 26.3 per cent improved, and one or 2.6 per cent unimproved (Table IV).

Other pathologic findings encountered in this series are of interest in regard to end-results. Retroversion was encountered in 57 cases; 39 occurred in the group of "partially infected cones," 18 in the "completely infected group." The end-results in these cases coincide strikingly with patients free from uterine displacement. Salpingitis was found in 12 patients. Per se it has no direct effect on cure of cervicitis. When combined with endometritis and a "completely infected cone," it aids the proof of infection in the retained endocervical segment as previously shown. Continued reinfection from Skene's or Bartholin's glands may be anticipated in the gonorrheal form. In 12 cases of cervicitis associated with salpingitis, cure occurred in only 50 per cent of the cases. Two failures occurred in "partially infected cone group," and 4 in the completely infected cone group.

The symptomatic results after excision of the cervix are in a measure interwoven with anatomical results but operative infection and trauma remain paramount. In three cases severely infected, sloughing of the flaps occurred exposing the cervical stump. Healing was protracted and the cervix remains irregular and deformed. Symptoms persist. In two other patients partial retraction of the anterior flap was due to cutting of the central suture. As these were radium cases, removal of the cervical pack and radium were no doubt causative. The partially exposed stumps were ultimately covered, but discharge persists in spite of a well healed portio. In the remaining twenty-two failures in this series there is no apparent anatomical defect causative of discharge.

The following tables summarize the series:

Table I consolidates the results in the three cone groups of the entire series; 103 or 79.2 per cent were cured, 23 or 17.7 per cent improved, and 4 or 3.1 per cent were unimproved. In 9 or 6.9 per cent there was recurrence nine to twenty-four months after operation.



TABLE I. TOTAL SERIES

TYPE OF CERVIX	NO.	CURED	IMPROVED	UNIMPROVED	RECURRENCE
Low infection	47	40	6	1	4
Intermediate infection	45	36	7	2	4
Complete infection	38	27	10	1	1
Total	130	103	23	4	9
Percentage Total		79.2%	17.7%	3.1%	6.9%

TABLE II. LOW INFECTION GROUP

LENGTH OF CONE	0-10 MM.	11-20 MM.	21-30 MM.	31-40 MM.	41-50 MM.	TOTAL
No. of cases	1	8	21	12	5	47
Dilatation and curettage	2	3	7	3	1	16
Dilatation and curettage and insertion of radium			2	1		3
<i>Postoperative Complications</i>						
Hemorrhage						0
Infection					1	1
<i>End Results</i>						
Cured	1	6	17	11	5	40
Per cent cured	100%	75%	81%	91.6%	100%	85.1%
Improved		2	3	1		6
Per cent improved		25%	14.3%	8.4%		12.8%
Unimproved			1			1
Per cent unimproved			4.7%			2.1%
Recurrence		2	1	1		4
Per cent recurrence		25%	4.7%	8.4%		8.7%

Table II analyzes the "low infection cones," graded according to length. End-results are best in this group. In a total of 47 cases, 40 or 85.1 per cent were cured, 6 or 12.8 per cent improved, and 1 or 2.1 per cent unimproved. Four patients had recurrences; the earliest, one year after operation. The poorest results were obtained in cones between 11 and 20 mm., the best results in those ranging from 31 to 40 mm. Radium insertion and curettage were performed in 19 of 47 cases, an incidence of 40.4 per cent.

Table III records the end-result in "intermediate infection cones." Of 45 patients, 36 or 80 per cent were cured, 7 or 15.5 per cent improved, 2 or 4.4 per cent unimproved. There were four late recurrences; the earliest after nine months; the latest after twenty-four months. In contrast to Table I, the highest incidence of cure was noted in cones between 11 to 20 mm., the lowest in the group between 31 to 40 mm. where 7 of 9 specimens were associated with curettage and radium insertion. Curettage and radium insertion were performed in 23 of 45 cases, an incidence of 49.1 per cent.

TABLE III. INTERMEDIATE INFECTION GROUP

LENGTH OF CONE	0-10 MM.	11-20 MM.	21-30 MM.	31-40 MM.	41-50 MM.	TOTAL
No. of cases	0	8	27	9	1	45
Dilatation and curettage		3	7	5		15
Dilatation and curettage and insertion of radium		1	4	2	1	8
<i>Postoperative Complications</i> Hemorrhage			1			1
Infection		1				1
<i>End Results</i>						
Cured		7	22	6	1	36
Per cent cured		87.5%	81.5%	66.7%	100%	80%
Improved		1	3	3		7
Per cent improved		12.5%	11.1%	33.3%		15.5%
Unimproved			2			2
Per cent unimproved			7.4%			4.4%
Recurrence		1	3			4
Per cent recurrence		12.5%	11.1%			8.9%

TABLE IV. COMPLETE INFECTION GROUP

LENGTH OF CONE	0-10 MM.	11-20 MM.	21-30 MM.	31-40 MM.	41-50 MM.	TOTAL
No. of cases	2	8	17	9	2	38
Dilatation and curettage	2	2	3	3	1	11
Dilatation and curettage and insertion of radium		1	2	1		4
<i>Postoperative Complications</i> Hemorrhage		1	1	1		3
Infection					1	1
<i>End Results</i>						
Cured	1	7	14	4	1	27
Per cent cured	50%	87.5%	82.4%	44.4%	50%	71.1%
Improved	1	1	3	4	1	10
Per cent improved	50%	12.5%	17.6%	44.4%	50%	26.3%
Unimproved				1		1
Per cent unimproved				11.1%		2.6%
Recurrence		1				1
Per cent recurrence		12.5%				2.6%

Tables IV and V tabulate the results in the "complete infection cones." Both operative contamination and preoperative infection of the residual endocervical strip militate against good operative results. Incidence of cure is lowest in this group. Of 38 cases, 27 or only 71.1 per cent were cured, 10 or 26.3 per cent were improved, and 1 or 2.6 per cent were unimproved. As in Table III, the poorest end-results were obtained in the group ranging between 31 and 40 mm. The incidence of curettage and radium insertion in this cone type is only 39.4 per cent. Six cases with residual endocervical segments infected before operation cause the poorest end-results. This is affirmed by seven cases of endometritis, seven cases of salpingitis, one case of cervical polyps and one of cervical fibroid as recorded in Table V.

TABLE V. COMPLETE INFECTION GROUP

<i>Pathologic Diagnosis of Cervix</i>		0-10 MM.	11-20 MM.	21-30 MM.	31-40 MM.	41-50 MM.	TOTAL
LENGTH OF CONE							
No. of cases		2	8	17	9	2	38
Subacute endocervitis				2	1		3
Subacute and chronic endocervitis		1	5	6	2	2	16
Subacute endocervitis with erosion	1°		1				1
	2°		1	6	3		10
	3°						0
Subacute and chronic endo- cervitis with erosion	1°						0
	2°	1	1	3	3		8
	3°						0
<i>Associated Pathology</i>							
Endometritis			1	5	1		7
Salpingitis			1	3	3		7
Retroversion			2	10	5	1	18
Cervical polyp				1			1
Cervical fibroid				1			1

Table VI shows the effect of the dilatation and curettage when performed prior to excision of cervix. Of 42 patients so handled only 71.4 per cent were cured, 10 or 23.8 per cent were improved, and 2 or 4.7 per cent were unimproved.

TABLE VI. DILATATION AND CURETTAGE

TYPE OF CERVIX	NO. OF CASES	CURED	IMPROVED	UNIMPROVED
Low infection	16	13	3	0
Intermediate infection	15	11	4	0
Complete infection	11	6	5	0
Total	42	30	12	0
Percentage total		71.4%	28.6%	

As shown in Table VII insertion of radium shows even worse end-results. Of 15 cases 8 or only 53.3 per cent were cured, 5 or 33.3 per cent were improved, and 2 or 13.3 per cent were unimproved.

TABLE VII. DILATATION, CURETTAGE AND RADIUM INSERTION

TYPE OF CERVIX	NO. OF CASES	CURED	IMPROVED	UNIMPROVED
Low infection	3	2	1	
Intermediate infection	8	4	3	1
Complete infection	4	2	1	1
Total	15	8	5	2
Percentage total		53.3%	33.3%	13.3%

Table VIII strikingly indicates the improvement after operation when curettage and radium insertion are omitted. Of 73 cases, 65 or 89.04 per cent were cured, 8.21 per cent were improved, and 2 or 2.75 per cent were unimproved.

TABLE VIII. NO DILATATION OR RADIUM INSERTION

TYPE OF CERVIX	NO. OF CASES	CURED	IMPROVED	UNIMPROVED
Low infection	28	25	2	1
Intermediate infection	22	21	0	1
Complete infection	23	19	4	0
Total	73	65	6	2
Percentage total		89.04%	8.21%	2.75%

Consideration of the facts presented in this paper warrants the following conclusions:

1. Pathologic examination of the excised cone, proves incomplete removal of the endocervix. Axiomatically, therefore, a segment of endocervix is retained after excision or amputation of the cervix.

2. In partially infected cervixes, healthy endocervix at the apex of the cones indicates a healthy endocervical segment retained above the level of transection. Surgical excision therefore has been adequate for clinical relief.

3. Clinical failure results from operative contamination and infection. The operations of dilatation and curettage and radium insertion performed simultaneously with cervical excision afford such infective opportunities. Vaginal packing for postoperative hemorrhage is also contributory.

4. In completely infected cones a healthy or infected segment of endocervix remains in situ. If healthy, operative infection leads to postoperative discharge as in the previous group. If infected before operation as can be gaged from concomitant endometritis, leucorrhea naturally

persists. Combination of both factors in this cone group leads to the poorest operative results.

In closing, thanks are extended to Dr. Morris Glass for aid in procuring the follow-up notes and Mr. James V. Dunn for the excellent tables.

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(For discussion, see page 145.)

## SYRINGOMYELIA COMPLICATING PREGNANCY AND LABOR WITH REPORT OF A CASE\*

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**O**RGANIC neurologic spinal cord conditions complicating pregnancy are rare. Among these complicating conditions which have been reported are meningitis, tabes, spinal cord tumors, Friedrich's ataxia and myelitis. Myelitis is probably the most common complication. The occurrence of any spinal disease raises the question of obstetric complications and deserves consideration. A search of the literature failed to disclose any reported cases of syringomyelia as a complication of pregnancy. We therefore considered our case worthy of report.

#### CASE REPORT

A twenty-seven-year-old para ii who presented fairly typical evidences of syringomyelia with the cavity in the central portion of the cervical and the upper dorsal regions of the spinal cord, had an uncomplicated pregnancy and presented no complication in labor that could be ascribed to the spinal lesion. The condition was checked to a considerable extent by x-ray treatment.

Mrs. J. H., aged twenty-seven years, admitted to the Graduate Hospital (Service of Dr. Elmer) on October 17, 1929, complaining of weakness and numbness in the left hand and weakness and stiffness in the left leg. Five months previously she noticed weakness of the little finger and shortly thereafter of the ring finger of the left hand. About two months before admission she also observed tingling in the back of the left hand extending sometimes as far as the elbow. In September, 1929, the patient noticed that her left leg was somewhat stiff and she limped when walking. There were no symptoms referable to any other part of the body. The patient had her last menstrual period on July 12, 1929. (Three months' pregnancy.)

The family history was irrelevant. The patient stated that she had had a fall in childhood and developed a spinal deformity which was treated by plaster of Paris jackets in Johns Hopkins Hospital at about the age of fifteen; with this treatment there was considerable improvement. In 1924, she was delivered of a

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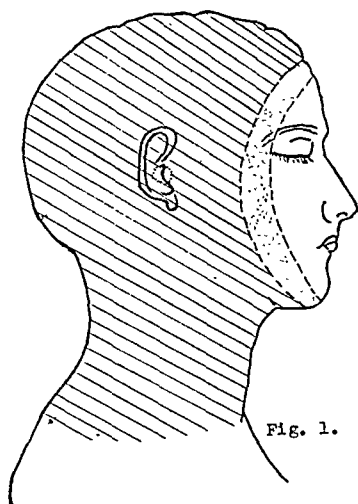


Fig. 1.

////// Anesthesia for pain and temperature

.... Diminution of sensibility to pain and temperature

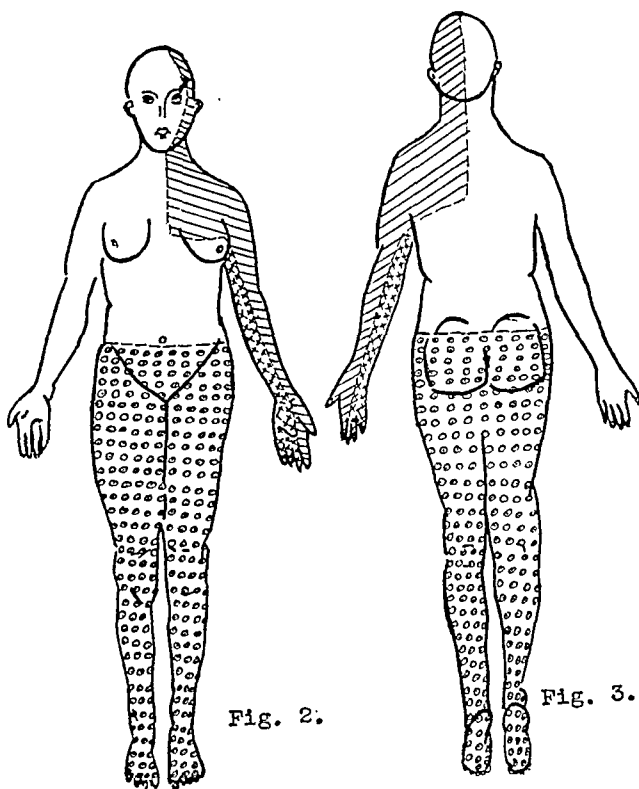


Fig. 2.

Fig. 3.

////// Anesthesia for pain and temperature

xxx Anesthesia for temperature only

ooo Loss of vibratory sense

normal baby without instrumentation; there were no miscarriages. Otherwise her past medical and personal histories were irrelevant.

*Examination.*—A well nourished woman of somewhat less than average mentality. There was a marked scoliosis of the dorsal lumbar region with the convexity to the right, x-ray examination showed that the straightest point was at the tenth dorsal vertebra and that the scoliosis was of functional origin. General physical examination was otherwise negative.

*Neurologic.*—There was a definite narrowing of the left palpebral fissure with enophthalmos; the left pupil was much smaller than the right (Horner syndrome). There was very slight weakness in the right hand and forearm. The left hand showed weakness in the interossei, in the opponens, and to a lesser extent in the flexors and extensors. The biceps and triceps reflexes were bilaterally absent. There was no weakness in any of the trunkal movements. The abdominal reflexes were active. The left lower extremity was somewhat rigid; the right about normal. In walking she dragged the left leg in a hemiparetic fashion. The knee jerk and achilles reflex were bilaterally exaggerated but much more so on the left side. There was a sustained ankle clonus and Babinski phenomenon on the left side. There were no sphincter disturbances. The synergic control was normal throughout. Sensory examination revealed a dissociated disturbance of sensation: there was complete loss of sensation for pain and temperature with complete preservation of sensation of touch over the following areas: the distribution of the left descending root of the fifth nerve; an area of anesthesia in the buccal mucosa about 1 by 1½ cm. in back of angle of the mouth; no corneal anesthesia; the left metameres from the first cervical to the first dorsal and somewhat less complete loss of pain and temperature over the left second, third and fourth dorsal metameres and over the right eighth cervical and first dorsal metameres (Figs. 1, 2, and 3). There was in addition, diminution of vibration sense in the left forearm. All other sensory examinations were negative.

The fundi and perimetric studies showed no abnormalities. The Barany tests were negative. The spinal fluid was under 10 mm. of Hg pressure and was normal in every respect. Blood Wassermann, blood chemistry, and urinalysis were negative. Erythrocytes, 3,470,000; hemoglobin, 61 per cent; leucocytes, 9,100; polymorphonuclears, 67 per cent; small lymphocytes, 26 per cent; transitional, 6 per cent; eosinophiles, 1 per cent.

*Course.*—During her brief residence in the hospital the patient burnt the left arm leaning against a hot radiator. The diagnosis of syringomyelia with a somewhat irregular cavity extending from the upper cervical to the upper dorsal regions was made. The patient was referred for x-ray treatment to Dr. G. E. Pfahler. She received 25 per cent dose on November 11, 1929, and seven doses at weekly intervals from May 2, 1930, to June 19, 1930, over the entire cervical and upper dorsal regions. Factors: 200 K.V.P. 4 Ma. 50 cm. distance ½ cu. and 2 aluminum filters, 18 minutes: about 23,000 units per treatment. There was apparently an arrest of the process, and possibly improvement in some respects.

*Obstetric Data.*—Feb. 1, 1930. Last menstrual period was July 12, 1930. Date of expected confinement therefore should be April 19, 1930. Except pain in left hand since the second month of pregnancy, patient does not have any complaints. Examination reveals patient to be in good physical condition. Blood pressure 120/80. Heart and lungs negative. Abdomen pendulous, about seven months pregnant, vertex presentation, fetal heart sounds heard. Pelvic measurements: spines 25 cm., crests 28 cm., external conjugate 20 cm. Vaginal examination: lacerated birth canal, very marked promontory. X-ray of the pelvis was made on Feb. 1, 1930, and the report was as follows: The measurement of the inner surface of the acetabulum to the opposite side was 16 cm. There appeared to be no bone deformity that would interfere with the normal pregnancy. The patient reported to the clinic only twice until her delivery.

On Feb. 15, 1930, a breech presentation was found and on March 15, 1930, a vertex again. Blood pressure, and urine were normal on all prenatal visits.

On April 3, 1930, sixteen days before the expected confinement, patient was admitted to the hospital, being in active labor. Her labor pains began at 5 P.M. April 2, 1930, and were mild through the night, but in early morning the pains began to get stronger and oftener. April 3, 1930, 10:20 A.M. on admission pains every five minutes, good uterine contractions. Abdomen very pendulous, head presenting and floating. Heart LLQ. Cervix about completely dilated and thinned out, head floating. A podalic version was performed without much difficulty and a living male child was delivered at 12:30 P.M. April 3, 1930.

Weight of child 8 pounds 5 ounces. A cervical and deep perineal tear were repaired immediately. Contractions of uterus after delivery were good, normal amount of postpartum bleeding. Placenta delivered spontaneously at 12:50 P.M. The whole duration of labor was nineteen hours fifty minutes. Puerperium afebrile, involution of the uterus normal. April 15, 1930, mother and baby discharged in good condition. Cervical repair and perineorrhaphy healed by first intention.

*Neurologic Reexaminations.*—April 29, 1930. Showed the disappearance of all anesthesia over the right forearm. There was improvement in power in the small muscles of the left hand. Otherwise findings were unchanged.

Sept. 12, 1930. Showed considerable improvement in power of the left hand and forearm.

Dec. 23, 1930. Considerable improvement in power of the interossei and opponens in the left hand. There appeared a loss of vibratory sensation in the left lower extremity up to the level of the iliac crests.

#### COMMENT

Syringomyelia, which is characterized pathologically by gliosis and cavitation about the central portion of the spinal cord, is not as common in women as in men. Thus, of 190 cases collected by Schlesinger<sup>1</sup> there were only 57 women of whom 37 were between the age of twenty and forty. There is no record of any patient being pregnant after the development of syringomyelia.

From an obstetric standpoint, this patient presented, at the time of admission to the hospital, two problems: one, whether or not the product of gestation would go on to term and if pregnancy would aggravate the syringomyelic process, and two, whether or not complications could be anticipated in labor.

There was no reason to think that the syringomyelia would in any way interfere with the normal development of the fetus for the disease is never toxic; even if it is neoplastic, as is thought by some, it is not accompanied by metastasis. Furthermore, the growth of the fetus is not dependent upon the spinal cord. Goltz and Freusberg<sup>2</sup> sectioned the spinal cord of a nine-months-old dog. Later, the animal conceived and went through normal pregnancy and labor. Lapinsky<sup>3</sup> demonstrated in his experiments on animals that when the uterus is completely isolated from the spinal cord, and all nerve connections with higher centers are abolished, it may become gravid and delivery may occur at the normal period. Not knowing how pregnancy may affect syringomyelia, termination of gestation was advised against. It was therefore felt that the gestation can go uninterrupted to term.

The second question, as to the possibility of difficult labor, was perhaps somewhat more difficult to answer, for disease of the spinal cord in pregnancy is not common. The majority of the cases of myelitis and tumors recorded occurred in the puerperium and did not present a problem of labor. From the cases reported in which the spinal disease preceded labor, it was evident that if the lesion occurred above the sacral segments, which innervates the uterus, no trouble was experienced. Thus in the cases reported by Robinson<sup>4</sup> there was a transverse myelitis in the dorsal region with incontinence of urine and feces, yet the labor was at term,



spontaneous and *painless*, with normal uterine contraction but without the action of the abdominal muscles. A somewhat similar case with a spontaneous painless labor was reported by Meyer.<sup>5</sup> In this case there was a transverse myelitis in the upper dorsal region due to an intramedullary tumor. Another case of a spinal cord tumor of three years' duration with a complete paralysis below the waist and a normal spontaneous but painless delivery was reported by Jackson.<sup>6</sup> Also in cases of transverse myelitis of traumatic and tubercular origin, spontaneous painless labor is the rule as demonstrated in the three cases quoted by Vaeth,<sup>7</sup> with lesions in the cervical and upper dorsal regions; by Lange<sup>8</sup> in the dorsal area; by Anna Lenkas<sup>9</sup> and by Krueger and Offergold<sup>10</sup> with a lesion in the lower dorsal vertebrae and second lumbar vertebrae (2 cases). On the other hand, where the lesion is located in the sacral area as in the case reported by Schumann and Fist,<sup>11</sup> there may be serious interference with labor. In this case the woman was ten months pregnant, there were no uterine contractions and the patient died of sepsis. Taylor<sup>12</sup> reports a case of myelitis due to a tumor involving the lumbar enlargement and extending into the cauda equina with paraplegia and loss of sphincter control. In this case the pregnancy went on to term but the uterine contractions were lacking and instrumental delivery became necessary.

The involvement of the posterior columns does not appear to interfere with labor. Thus, tabes complicating pregnancy and labor have been reported by a number of observers: (Gaussel-Ziegelmann,<sup>13</sup> Pitres,<sup>14</sup> Fruhinshalz and Remy,<sup>15</sup> Dufour and Cottenot,<sup>16</sup> Grenier,<sup>17</sup> Theis,<sup>18</sup> Jacob,<sup>19</sup> Allen,<sup>20</sup> Williams<sup>21</sup>) all agree that the effect of tabes on pregnancy is not great. All authors seem to agree that tabes does not interfere seriously with labor, that labor is painless and is apt to be precipitous (Williams<sup>21</sup>) but that the patients are unable to use the abdominal muscles to aid the expulsion of the child. It should be borne in mind that tabes is preeminently a disease of the sensory and not of the motor apparatus.

Acute anterior poliomyelitis in which the lower motor neuron is involved likewise shows no serious problem in labor. Thus Schmidt<sup>22</sup> reports a case of a pregnant woman who developed incomplete diffuse flaccid paralysis of all four extremities and had a spontaneous painless delivery of a stillborn child. Miller<sup>23</sup> reports two cases one of which developed paralysis of both lower extremities and abdominal muscles, yet had a spontaneous delivery with normal uterine contractions but no assistance of the abdominal muscles. The other case developed a septic cystitis and required a hysterectomy. Foulkrod<sup>24</sup> also reports a case of poliomyelitis with spontaneous painless delivery of a stillborn child. Normal delivery seems possible in chronic forms of anterior horn cell involvement as in the cases reported by Fleischman,<sup>25</sup> Litschkus<sup>26</sup> and Gutzmann.<sup>27</sup> Some of these cases required assistance in the second stage of labor due to weakness of abdominal muscles. Spontaneous delivery was reported in amyotrophic lateral sclerosis by Jardine,<sup>28</sup> in Landry's paralysis by Davidsohn,<sup>29</sup> and in Friederich's Ataxia by Alpers and Palmer.<sup>30</sup>

Thus a review of the clinical literature tends to show that if the transverse spinal lesion is above the sacral segments, there should be no difficulty with uterine contractions; and if the lesion be in the upper dorsal or cervical segments, there is no interference with the voluntary action of the abdominal muscles. In the involvement of the posterior columns as in tabes the labor is not only spontaneous and painless but often precipitous and this in the absence of voluntary muscular assistance. In transverse lesions in the sacral area and in destructive lesions of the anterior horn cells in the lower spinal segments, as in acute anterior poliomyelitis, and amyotrophic lateral sclerosis, the first stage of labor

is usually unimpeded, but the second stage may require surgical assistance.

In our case, the cavity was located in the cervical and upper dorsal region, a considerable distance from the points of innervation of both the abdominal muscles and the uterus. It was, therefore, felt, that in a case of this sort, the uterine contractions, as well as the perineum and abdominal walls would function normally. This proved to be the case. It is hard to foretell what would occur if a similar cavity were located in the sacral area. Whether or not spontaneous delivery can take place in the total absence of spinal cord innervation in the human being, is questionable. Experimental evidence tends to show that this may be possible.

Simpson<sup>21</sup> as long ago as 1871 observed in a sow that spontaneous birth could take place after destruction of the dorsal and lumbar cords. Cushny<sup>22</sup> concluded from his observation on animals that the contraction of the uterus on mechanical or electrical stimulation were purely myogenic and not nervous in origin. Holste<sup>23</sup> reported rhythmic spontaneous contraction of the musculature of the excised uterus of the guinea pig. Rein<sup>24</sup> reported the spontaneous birth of the young in the rabbit following section of all extrinsic nerves of the uterus. Kurdowsky<sup>25</sup> showed that parturition could take place from the uterus of a rabbit after extirpation, thus eliminating the influence of the central nervous system or the prevertebral ganglia. Thus far experimental evidence tends to show that uterine musculature, like other smooth muscle, possesses the inherent capacity of undergoing rhythmic contraction. Moreover experimental evidence shows that uterine contractions are augmented by stimulation of the sympathetic (through the hypogastricus which takes its origin from lower dorsal and upper two lumbar nerves) and is inhibited by the parasympathetic (through the pelvius which arises from the sacral autonomic cord). In transections of the cord producing paralysis of the lower half of the body, spontaneous parturition proceeds with abnormal rapidity and vigor. That the volume of the uterine cavity is definitely influenced by cerebral activities was shown by Bourber and Copenhagen.<sup>26</sup> It would therefore appear that the uterus, in addition to its myogenic properties is subject to motor and inhibitory influences of reflex and central nervous origin (Zimmerman<sup>27</sup>). This explains the precipitous labor in the tabetic and the augmentation of the uterine contractions observed during cesarean section made under spinal anesthesia (Williams<sup>28</sup>).

Despite the experimental evidence and in view of the more complicated organization of the human body, the question of spontaneous labor in destructive lesions of the lower portion of the spinal cord must for the present remain undecided. Clinical evidence, as revealed by the cases reported by Schumann and Fist<sup>11</sup> and by Taylor<sup>12</sup> tends at least in part to contradict the experimental findings.

The effect of deep x-ray therapy proved beneficial in our case. This mode of treatment was introduced by Raymond in 1905. The largest number of cases was reported by Heinisman and Czerny.<sup>29</sup> These authors report not only an arrest of the process in many cases, but a definite improvement in motor, sensory, and trophic disturbances in many of their patients. The mode of action of the rays is not clear; it probably acts by destroying the gliosis preventing pressure and cavitation.

## SUMMARY

A case of syringomyelia, with a cavity in the cervical and upper dorsal regions complicating pregnancy, and presenting no complications in labor that could be ascribed to the spinal disease, is reported.

Experimental evidence leads us to believe that in lower animals, the uterine contractions of labor are purely myogenic, and that pregnancy and spontaneous rapid labor can occur when all nervous connections of the uterus are severed. Under normal conditions, the uterus is influenced by the central nervous system through its extrinsic nerves.

The review of the clinical and pathologic literature shows that pregnancy and labor are largely independent of spinal cord disease. Spinal cord disease, in the absence of other complications, need not be a cause for termination of pregnancy. In tabes and in transverse lesions above the lumbosacral cord enlargement despite the lack of voluntary abdominal muscle action, the labor is apt to be not only spontaneous but precipitous; in disease of the anterior horn cells as in poliomyelitis in the lumbosacral region and in transverse lesions of the sacral area, obstetric assistance may be required although these lesions do not abolish the uterine contractions.

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## AN ANALYSIS OF A SERIES OF 82 CASES OF ECTOPIC PREGNANCY\*

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IN 1851, Charles D. Meigs,<sup>1</sup> Professor of Midwifery, and the Diseases of Women and Children, in Jefferson Medical College, described with punctilious accuracy a series of cases of ruptured ectopic pregnancy, the symptoms, signs, and gross pathology of which might have been written for a textbook of today. There the similarity ends as evidenced by this quotation, pathetic when considered in the light of our present day opportunities. He said "What, alas, can we do in these cases? We could make an incision in the abdomen, and clear away the coagula and the serum. But who is he bold enough to do so? Who is he astute enough to discriminate betwixt all the possible causes of such phenomena with so much clearness as to warrant him in the performance of a gastrotomy for fallopian pregnancy? There is no such wise and bold surgeon; and, therefore, nothing remains for us but to extend all the relief within the narrow boundaries of our power, and calmly await and submit to the inevitable end. Such are painful scenes to the sensitive mind. They cast a color of gloom over the pathway of the medical man, whose whole walk, indeed, is among those who are in pain, in weakness, in fear, or in the valley of the shadow of death. A physician may be calm, and even cheerful, but a merry doctor is a very singular phenomenon."

Schumann,<sup>2</sup> in his entertaining chapter on the historical consideration of ectopic pregnancy, notes that Parry as late as 1876, held convictions equally as dismal when considered in the light of present day knowledge, although he pointed the way to a possible remedy by "gastrotomy." Even today, with the advantages of modern surgical technic at our command, the "enigma of ectopic pregnancy," as Danureuther<sup>3</sup> has termed it, confronts us as a diagnostic problem, oftentimes puzzling in its solution. With the thought of contributing to the literature on the subject, we are presenting an analysis of a series of 82 consecutive cases of ectopic pregnancy as observed on the Gynecological Service of Dr. Brooke M. Anspach, at Jefferson Medical College Hospital from September, 1921 to September, 1931.

*Incidence.*—Eighty-two cases of ectopic pregnancy occurred among 3,747 admissions to the Gynecological Ward, representing an incidence

\*Read at a meeting of the Obstetrical Society of Philadelphia, November 5, 1931. For lack of space, this article must be abridged, but the complete article is included in the authors' reprints.

of 2.19 per cent in relation to gynecologic cases. Wynne,<sup>4</sup> at Johns Hopkins Hospital, reported an incidence of 1.3 per cent, while Urdan<sup>5</sup> reported 1.5 per cent at Mt. Sinai Hospital, New York. Schumann has estimated the incidence in relation to intrauterine pregnancy to be 1 to 303, or 0.33 per cent.

*Age.*—The youngest patient was twenty years of age, and the oldest, forty-two. Sixty-one of the cases occurred between the ages of twenty-three and thirty-five years, 74.3 per cent. Forty-six were between the ages of twenty-four and thirty-three years, 56 per cent. Schumann quotes 60 to 70 per cent as occurring between the latter ages, as do other observers.

*Etiology.*—Speculation as to the contributing causes of ectopic pregnancy is as rife today as ever. Out of the maze of conflicting opinions, one concrete thought stands out, namely, that there is some interference with the passage of the ovum, fertilized or unfertilized, in its journey from the fimbriated extremity of the tube to the uterine cavity. This may be developmental, perhaps associated with hypoplasia or abnormalities. It may be due to pressure upon or distortion of the lumen from without, the result of new growths in the adnexa or uterus, or by virtue of peritubal adhesions, postoperative or postinflammatory. Finally, the most frequently assigned factor is an obstructive change within the tubal lumen, the result of prior salpingitis of varying degree.

In the nulliparous woman, the occurrence of ectopic pregnancy suggests a developmental defect if she has been married fairly recently. If conception has occurred relatively late in her married career, with a likely history of an earlier genital infection, then inflammatory changes in the tube must be considered. Previous operations play their part from the point of view of postoperative adhesions.

In the parous woman, the probability of an inflammatory cause is greater, especially with a definite history of abortions, postpartal infection or intercurrent genital tract disease. So-called lengthy "sterility," or "one child sterility," periods were previously thought to be indicative of long-standing inflammatory changes resulting from infection, sufficient regeneration having occurred to permit the fertilized ovum to enter the tubal lumen, only to have its progress impeded by an occluded area. Recent analyses of numerous series of cases by different observers fail to substantiate this protracted period of infertility.

With these considerations in mind, it is interesting to note the result of our observations with respect to the following possible etiologic factors.

#### 1. REPRODUCTIVE AND MARITAL HISTORY

No pregnancies occurred in 16 patients, 19.5 per cent. Seven had been married for three years or less when the ectopic pregnancy occur-

red. Eight patients had been married from five to fourteen years, and if we consider that long a period as one of "absolute sterility," indefinite as the phrase is, the occurrence of it in the entire series would be about 10 per cent, the same figure ascribed to the general incidence of sterile marriages. (In 1 case the lapse of time was undetermined).

There had been one previous pregnancy in 21 patients, 25.6 per cent, when the ectopic occurred. Thirteen of these pregnancies had been full term, 3 ectopic, and 5 had resulted in abortion. Eleven of the ectopics occurred within five years of the previous pregnancy, while 7 happened from five to sixteen years afterward, indicating a "one child sterility" of 8.8 per cent; somewhat less than the incidence of 10 to 12 per cent usually mentioned. (In 3 cases, the lapse of time was undetermined.)

Multiple pregnancies had occurred in 45 patients, 54.9 per cent, the majority of the ectopics in this group (79.4 per cent) happening within five years of the last intrauterine pregnancy, with but 4 cases occurring later than six years afterward.

The shortest period elapsing after an intrauterine pregnancy and the occurrence of the ectopic was four months and the longest period was twenty years, an average time of four years and four months. Five patients had previous ectopics, an incidence of 6.09 per cent. Incidences ranging from 4 to 16 per cent have been reported.

The above figures emphasize two points particularly. First, that in the fertile woman a long period of infertility preceding an ectopic pregnancy is not the rule, and second that as parity increases, the incidence of ectopic pregnancy increases, indicating perhaps, that the greater the number of pregnancies, the greater the possibility of tubal obstruction.

## 2. HISTORY OF INFECTION

The histories of 25 patients suggested the possibility of old pelvic infection, neisserian, postabortal, or postpartal, 30.5 per cent, of which half were probably of gonorrheal origin. In 30 patients, one or more miscarriages had occurred prior to the ectopic pregnancy, at least 6 of which had been induced. (Two-thirds of the patients had full-term pregnancies as well.) This represents 36.5 per cent of the entire series, and 46.9 per cent of the multiparae. The incidence of abortions in multiparae in general has been estimated by different observers to be anywhere from 20 to 50 per cent. Lesions of postabortal, postpartal, or neisserian origin are potential instigators of peritubal adhesions and tubal occlusion.

## 3. HISTORY OF PREVIOUS OPERATIONS

The importance of the history of a previous operation as a possible etiologic factor was emphasized in this analysis, because 23 patients, 28 per cent, had had abdominal or pelvic surgery performed, while 8 had

had intrauterine procedures, a total of 37.7 per cent. This high incidence corresponds to the recently reported statistics of Urdan<sup>5</sup> and Lavell.<sup>6</sup> About one-third of the operations had been performed for pelvic inflammatory conditions of varying degree, but the fact that the remainder of the procedures were noninflammatory in character, does not exclude the occurrence of subsequent adhesions. A point of further enlightenment is that in two-thirds of the patients operated upon, no intervening pregnancy occurred prior to the ectopic gestation, indicating perhaps, a lessened opportunity for normal impregnation to occur in these patients. (Table I is descriptive of the previous operations.)

TABLE I. PREVIOUS OPERATIONS

Appendectomy	7 Cases
Salpingo-oophorectomy	3 Cases
Salpingo-oophorectomy and appendectomy	3 Cases
Salpingectomy	2 Cases
Salpingectomy and appendectomy	1 Case
Adhesions (previous salpingo-oophorectomy)	1 Case
Pelvic adhesions and appendectomy	1 Case
Posterior colpotomy	1 Case
Plastic, uterine suspension and appendectomy	2 Cases
Cesarean section and subsequent appendectomy	1 Case
Cesarean section, extraperitoneal	1 Case
Total	23 Cases—28 per cent
Dilatation and curettement (1 or more)	8 Cases
Total	31 Cases—37.7 per cent
(5 of the operations had been for previous ectopic pregnancy)	

#### 4. DEVELOPMENTAL ANOMALIES AND NEW GROWTHS

In but 2 patients could developmental anomalies be demonstrated conclusively. In one patient an accessory tubal ostium was present in the pregnant tube, while in another patient, para ix, a bicornuate uterus was found. As will be noted later, ovarian and uterine newgrowths were disclosed in 7 patients at the time of operation, 8.5 per cent.

#### RÉSUMÉ

No dependable etiologic factor was disclosed by the history in 27 cases, 33.0 per cent. Twenty-five patients, 30.5 per cent, gave a suggestive history of old pelvic infection, postabortal, postpartal, or neisserian in origin. This group was contributed to by those patients who had previously been subjected to intrauterine procedures. Of 23 patients, 28 per cent, having abdominal or pelvic surgery, 7 (8.5 per cent) were distinctively of an inflammatory nature. The possibility of postoperative changes involving the tubes in so large a proportion of the patients in the series must be borne in mind as additional causative incidents. The presence of ovarian and uterine newgrowths, disclosed at operation, in 8.5 per cent of the patients, may have influenced the etiology in those particular cases.

## CHIEF COMPLAINTS AT TIME OF ADMISSION

Pain of some variety in the pelvis or abdomen, was a chief complaint, and was present in all cases upon admission, being combined with vaginal bleeding in 64.6 per cent of all cases. In 15 patients there was a varying degree of shock, but in 9 cases pain was the sole symptom. Nausea and vomiting were noted in but 5 cases. In Urdan's series, 2.7 per cent experienced no pain.

1. *Pain*.—The first symptom of pain was experienced either on the day of admission or within thirty-five days prior to admission in 66 cases, 80 per cent. In 5 the time was indefinite, while in 11 cases, pain had first been experienced from thirty-five to eighty-five days before admission. In 28 per cent of the patients the initial pain was followed by subsidence for a period of one to three weeks, when recurrence occurred. The initial occurrence of pain as a symptom is detailed in Table II.

TABLE II. APPEARANCE OF FIRST PAIN PRIOR TO ADMISSION

	CASES	
Undetermined	5	
Day of admission	10	
1-5 days prior to admission	18	} 80 per cent
5-20 days prior to admission	20	
20-35 days prior to admission	18	
35-50 days prior to admission	4	
50-65 days prior to admission	5	
65-85 days prior to admission	2	
(Initial pain was followed by subsidence and recurrence in 28 per cent)		

2. *Menstrual History*.—Considerable difficulty was encountered, in determining the last regular period. Quite often patients interpreted "spotting" as menstruation, particularly when it occurred at the time of an expected period. Patient inquiry is required to elicit this information correctly.

\* \* \* \*

The menstrual history, prior to the occurrence of the present illness, had been regular as to periodicity in 65 cases, 79.2 per cent; irregular in 15 cases, 18.2 per cent; undetermined in 2 cases (2.6 per cent). These findings parallel Behney's<sup>7</sup> figures, and would indicate the important fact that in 4 out of 5 cases of ectopic pregnancy, the previous menstrual history is likely to be regular (Table III).

3. *Syncope*.—Syncope occurred in 22 patients, 26.7 per cent, either at the time of admission or some time before. Behney reported the condition in 24 per cent of his series. This symptom, occurring in over one-



quarter of a series of cases, is valuable when associated with pain and irregularity of menstruation.

\* \* \* \*

TABLE III. MENSTRUAL HISTORY

	CASES	PER CENT
Indefinite (irregular bleeding occurring)	6	7.3
No "missed" period	10	12.2
"Spotting" prior to expected period	10	30.5
"Spotting" at time of expected period	15	
Period overdue 1 week or less	10	45.1
Period overdue 2 weeks or less	7	
Period overdue 3 weeks or less	4	
Period overdue 5 weeks or less	4	
Period overdue 6 weeks or less	2	
Period overdue 8 weeks or less	10	4.8
Period overdue 10 weeks or less	2	
Period overdue 11 weeks or less	1	
Period overdue 15 weeks or less	1	
<i>Previous Menstrual Type</i>		
Regular as to periodicity prior to ectopic pregnancy	65 Cases—	79.2 per cent
Irregular as to periodicity prior to ectopic pregnancy	15 Cases—	18.2 per cent
Undetermined	2 Cases—	2.6 per cent

#### ABDOMINAL FINDINGS

Abdominal tenderness was exhibited by 70 patients, 85.3 per cent. It was generalized in 21 cases and localized in 49, about equally distributed between the right and left lower quadrants, and the lower abdomen. Tenderness was absent or not noted in 12 cases, 14.7 per cent.

Rigidity was present in 34 cases, 41.4 per cent. It was generalized in 10 patients and localized in 24. It was absent or not noted in 48 cases, 58.6 per cent.

Dullness in the flanks was demonstrated in 12 patients, 14.7 per cent. Marked intraabdominal hemorrhage was present in all these patients. An abdominal mass was palpable in 12 patients.

No observation of Cullen's sign was noted.

#### PELVIC FINDINGS

About two-thirds of the patients were examined vaginally either before operation or under anesthesia. In the remainder, pelvic examination was dispensed with because the diagnosis was obvious and treatment urgent or because examination had been made prior to admission. Masses or definite fullness were found in 42 cases, 51.2 per cent. Pelvic tenderness was present in 31 cases, 37.8 per cent. An enlarged uterus was noted in only 16 cases, 19.5 per cent, as was a tender or softened cervix (not necessarily in the patients having an enlarged uterus).

\* \* \* \*

TABLE IV. ANALYSIS OF BLOOD COUNTS

HEMOGLOBIN:	CASES	PER CENT
Above 85	5	6.0
55-85	49	60.0
Below 55	27	32.7
Not noted	1	1.3
RED BLOOD CELLS:		
Above 4 millions	18	22.0
Between 2½ and 4 millions	44	53.7
Below 2½ millions	8	9.8
Not noted	12	14.5
WHITE BLOOD CELLS:		
3 to 8 thousand	18	22.0
8 to 11 thousand	32	39.0
11 to 15 thousand	15	18.3
15 to 20 thousand	8	9.8
Over 20 thousand	7	8.5
Not noted	2	2.4

\* \* \* \*

TABLE V. BLOOD PRESSURE, TEMPERATURE, PULSE

	TWENTY-FOUR-HOUR CASES	DELAYED CASES	INCORRECTLY DIAGNOSED CASES	PER CENT
<i>Systolic Blood Pressure:</i>				
100-140	20	22	17	72
Under 100	16	1	1	20
No record	5	0	0	8
<i>Temperature:</i>				
98°-100°	25	18	15	70.8
Over 100°	2	4	3	11.7
Under 98°	14	1	0	18.3
<i>Pulse:</i>				
70-110	24	20	14	70.0
110-140	15	3	4	26.8
Not recordable	2	0	0	3.2

## SEDIMENTATION TEST

Our experience with the sedimentation test in ectopic pregnancy has been limited to 20 cases. The test is used routinely on the gynecologic service and is favorably regarded as an indicator of the activity of pelvic infection. We employ the graphic method of Cutler as modified by Stimson and Jones,<sup>8</sup> and are convinced of its practical application.

In those patients operated upon within twenty-four hours, the rapidity of sedimentation in all but one case closely approximated that seen in pelvic inflammatory disease. Free blood and clots were present in all these cases, thus explaining the rapid rate. In patients in whom operation was delayed, the sedimentation rate was similar.

The test was performed in 5 patients in whom the preoperative diagnosis was incorrect, the rate being rapid where rupture or abortion had occurred, while in 2 unruptured cases, the rate was slow. It would seem from this rather limited observation, that the chief value of the test lies

in the differentiation of an unruptured ectopic pregnancy from pelvic inflammatory disease, while in a fairly early rupture with pelvic hematocoele the test would aid in differentiating the latter from pelvic abscess. Where superimposed infection has occurred in an hematocoele, the rate differs little from that seen in inflammatory disease. These conclusions approximate those of Lavell and others.

#### HORMONE TEST FOR PREGNANCY

The female sex hormone test for pregnancy as developed by Mazer and Hoffman,<sup>9</sup> was employed in 2 cases, both of which proved to be ruptured tubal pregnancies. It was positive in both. Reports of the high percentage of accuracy being observed in this test points to its application as a diagnostic aid in indefinite, suspected cases of ectopic pregnancy.

#### DIAGNOSIS

Correct diagnoses were made preoperatively in 63 cases, 78.7 per cent. Excluding the cases of two individuals who succumbed before surgery could be performed, 40 patients (50 per cent) were operated upon immediately or within twenty-four hours of admission, while in 23 patients (28.7 per cent), operation occurred twenty-four hours or later after admission. The preoperative diagnosis was incorrect in a group of 17 patients, 21.3 per cent.

In those cases, operated upon immediately or within twenty-four hours, little difficulty was encountered in diagnosis, the symptoms and signs being clear-cut and urgent. In those patients operated upon after twenty-four hours, delay was occasioned by nonurgency of the symptoms, with no evidence of continued hemorrhage, thus allowing improvement in condition. Of the 17 undiagnosed cases, 2 were transferred from the general surgical ward, after consultation, where they had been admitted as acute appendices; 5 were thought to be pelvic inflammatory disease; 3 were diagnosed as incomplete abortion, abdominal section immediately following the dilatation and evacuation and examination under anesthesia in 2 cases. In 1, however, dilatation and evacuation was performed in error, followed in seven days by an intraligamentous rupture. Subinvolution and retroversion was the diagnosis in 3 cases; a myoma or a dermoid cyst was suspected in 1 case, while 2 study cases were exploratory in nature, and 1 case was simply prepared for a plastic operation at which time an abdominal section was decided upon because a pelvic mass was discovered. In about half of the cases therefore, the diagnostic error was caused by confusing the true condition with either pelvic inflammatory disease or incomplete abortion.

#### OPERATIVE FINDINGS

The ectopic pregnancy occurred 39 times on the right side and 43 times on the left side. Eleven were unruptured tubal gestations, 53 were

tubal ruptures, and 16 were tubal abortions. Two were intraligamentous. The proportion of tubal rupture to tubal abortion was 3.3 to 1, a finding similar to Lavell's, but somewhat at variance with the observations of others. Considerable argument might be attached to the interpretation of the pathology disclosed, unless it is remembered that the situations were observed by different operators, whose estimation of the lesion might differ.

Free blood and clots were found in two-thirds of the cases, and hematomas or clots in the remainder, except in the unruptured or slightly leaking cases.

Abnormalities of the opposite adnexa were noted in 32 cases, 39.1 per cent. In 11 patients the adnexa had been totally or partially removed, while in 11 cases the tubal lesion was inflammatory (13.2 per cent of the entire series). Ovarian abnormalities were present in 10 patients. One bicornuate uterus was seen, myomas were present in 4 cases, while a retroverted adherent uterus was present in one case and a previously suspended uterus in another. (Seven cases showed uterine abnormalities, 8.5 per cent.) The total percentage of pelvic abnormalities was 47.6. Behney reported practically the same percentage of abnormalities in his series. Pelvic and omental adhesions were present in 24 cases. It was impossible to state in some instances whether they were preexisting lesions, or the result of the ectopic pathology.

#### OPERATIVE TREATMENT

Preliminary uterine exploration was carried out in 22 cases, for the purpose of noting the position of the uterus, or for excluding an incomplete abortion.

Posterior colpotomy, as a diagnostic measure, was performed in 10 cases.

Either salpingectomy or salpingo-oophorectomy was performed in 52 cases, 65 per cent. Corrective pelvic surgery was performed additionally in 21 cases, 26.2 per cent, while in 7 cases, 8.7 per cent, supravaginal hysterectomy was necessary. The largest group corresponds roughly to those cases operated upon within twenty-four hours or soon afterward, while those cases requiring more extensive surgery were the delayed or incorrectly diagnosed cases.

Autotransfusion was performed in 15 cases, one resulting fatally. This patient had attempted an instrumental abortion prior to admission, death resulting from a streptococcic blood stream infection. Our feeling was that the autotransfusion contributed to the outcome, and since then we have abandoned the procedure if there is any question of infection. Intravenous saline infusion is used routinely if necessary and blood transfusions (Unger method) are employed postoperatively when indicated.

## POSTOPERATIVE COMPLICATIONS AND POSTOPERATIVE DAYS

Table VI shows in detail the various postoperative complications encountered, 33.3 per cent or 19.2 per cent exclusive of wound infection.

When the emergency nature of most of the operations for ectopic pregnancy is considered, it is astonishing that the incidence of postoperative complications is not higher.

TABLE VI. POSTOPERATIVE COMPLICATIONS AND POSTOPERATIVE DAYS

	CASES	PER CENT
No complication	52	66.6
Complications	26	33.3
Wound infection—6 "B" and 5 "C"	11	
Phlebitis	3	
Pyelitis	2	
Pelvic peritonitis	2	
Pulmonary atelectasis (collapse)	1	
Unusual abdominal distention	2	
Severe secondary anemia	1	
Unexplained fever (tuberculosis in 2?)	4	
		19.2 (Exclusive of wound infection)
Discharged within 19 days	55	70.5
Discharged 20-32 days	17	21.8
Discharged 33-49 days	6	7.7
(Average number of postoperative days, 20.7)		

## MORTALITY

There were 4 deaths in the series, a total mortality of 4.87 per cent. Two occurred before operation could be performed, and 2 were postoperative, an operative mortality of 2.5 per cent. Mortality rates have been reported, ranging from 0.97 per cent to 5.2 per cent (Farrar,<sup>10</sup> Lavell, Williams,<sup>11</sup> Urdan, Schumann, Bubis,<sup>12</sup> and Luker<sup>13</sup>).

Of the preoperative deaths, one occurred from hemorrhage on the way to the operating room from the receiving ward. The other patient was thought to be three months' pregnant and was admitted to the hospital for study because of gallstone colic. Amenorrhea had been present for three months and the patient knew that she was pregnant. "Spotting" was reported on the day of admission and no pelvic examination was made. Following an x-ray study, the patient suddenly collapsed and died from hemorrhage before operation could be performed. Autopsy showed that cornual rupture had occurred, a three months' fetus having been expelled into the abdominal cavity. A large number of gallstones were found in the gall bladder.

One postoperative case died on the third day presumably from the shock of the operation. The initial hemorrhage had been severe. No autopsy was secured.

The second postoperative death occurred on the eighth day from a streptococcus hemolyticus blood stream infection. This patient, as mentioned before, had attempted an abortion prior to admission to the

hospital and autotransfusion was employed at operation. Autopsy showed no peritonitis, and the organism was recovered from the heart chamber. The uterine cavity showed an acute suppurative endometritis.

#### ANALYSIS OF NONECTOPIC CASES

During the same period 69 patients suspected of having an ectopic pregnancy were admitted to the Service and these cases have been reviewed with interest.

Five patients were admitted with the positive diagnosis of ruptured ectopic pregnancy. In 36 patients the diagnosis was questionable but strongly suspected. In 17 patients the possibility of pelvic inflammatory disease or ectopic pregnancy was equally considered, while in 11 patients the differential diagnosis was between abortion and ectopic pregnancy.

There was a diagnostic error of 26 per cent in 17 operative cases. Four patients were operated upon within twenty-four hours as ruptured ectopics, 3 proving to be cases of pelvic inflammatory disease, while in one a loop of bowel had become strangulated after passing through an hiatus in the broad ligament. The patient was moribund and died on the operating table.

Thirteen patients were operated upon as suspected ectopics, twenty-four hours after admission or later. In 40 patients the diagnosis was revised after a period of observation, 2 of these patients being operated upon abdominally and 6 being subjected to an intrauterine procedure.

\* \* \* \*

The comparison of these two groups of cases brings to light the observation that the percentage of error encountered when operating upon cases thought to be ectopic, 26 per cent, was but little higher than that seen in those ectopic cases operated upon with an incorrect preoperative diagnosis, viz. 21.3 per cent. In the nonectopic group also, the diagnoses most frequently confused were, (1) pelvic inflammatory disease, (2) incomplete abortion. Posterior colpotomy, more frequently performed, would have lessened the operative error in those inflammatory cases subjected to abdominal section as ectopic gestations.

#### SUMMARY AND CONCLUSIONS

An analysis of a series of 82 consecutive cases of ectopic pregnancy revealed an incidence of 2.19 per cent in relation to gynecologic cases admitted.

There were 74.3 per cent of the patients between the ages of twenty-three and thirty-five years.

A prolonged period of "sterility" was not the rule prior to an ectopic pregnancy. With increased parity, the occurrence of ectopic pregnancy was likewise greater.

Etiologic factors were suggested (1) by a history of 30 per cent of old pelvic infections of neisserian, postpartal, or postabortal origin; (2) by a high incidence of prior operative procedures, 37.7 per cent; (3) ovarian and uterine newgrowths, disclosed at operation in 8.5 per cent of the patients. Mechanical obstruction to the passage of the ovum, the result of inflammatory or adhesive changes in or about the tubes was suggested by the history and finally by the operative findings in about two-thirds of the cases.

Abdominal or pelvic pain of some character was present in all cases.

Irregular vaginal bleeding or "spotting," either following a "missed period," or occurring prior to, or at the time of the next expected period, was reported by 88 per cent of the patients. The menstrual history, prior to the aberration caused by the ectopic pregnancy, was normal in 4 out of 5 cases.

Syncope occurred in one-quarter of the patients.

Concomitant signs of pregnancy were infrequent.

Abdominal tenderness was present in 85 per cent of the patients, less than half of them exhibiting rigidity.

Pelvic masses were present in half the cases with tenderness actually noted in only one-third.

A study of the blood counts, blood pressure estimations, temperature and pulse rates paralleled the findings of others, but the sedimentation test has not proved of definite differential value.

The proportion of tubal rupture to tubal abortion was 3.3 to 1.

There were 39.1 per cent of abnormalities noted in the opposite adnexa at the time of operation.

Autotransfusion has been abandoned in our treatment if there is any question of infection being present. Postoperative complications, with one exception, a collapsed lung, were not unusual in character and the postoperative days were not unusually prolonged.

A total mortality of 4.87 per cent and an operative mortality of 2.5 per cent have been presented.

Correct diagnoses were made in 78.7 per cent of the cases, the majority of the patients being operated upon immediately or within twenty-four hours. The preoperative diagnosis was incorrect in 21.3 per cent, a figure closely paralleling the diagnostic error of 26 per cent noted in a group of cases admitted as suspected ectopic pregnancies, operation disclosing other pathology. Certain features peculiar to either group have been pointed out. Comparison of the two series of cases revealed that pelvic inflammatory disease was the diagnosis most likely to be confused with ectopic pregnancy, incomplete abortion being next in order of frequency.

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(For discussion, see page 150.)

## THE USE OF SODIUM AMYTAL IN LABOR\*

### A PRELIMINARY REPORT

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OUR interest in sodium amytal in labor was aroused by a very optimistic report by Morehead and Mussey<sup>1</sup> of the Mayo Clinic. These authors reported 46 cases in which they gave three grains of sodium amytal by mouth when the cervix was effaced and two centimeters dilated. They claimed that most of their patients had good analgesia and relaxation of the soft parts. They observed no ill-effects on the babies and no prolongation of labor.

More recently, Hamblen and Hamblin<sup>2</sup> reported a series of 50 cases in which they gave sodium amytal by mouth in doses of from 9 to 18 grains. They found that when the initial dose was 9 grains, the patient derived very little benefit, but when the initial dose was 15 or 18 grains, the majority of their patients had excellent analgesia and amnesia.

Morehead and Mussey's article and the one by Hamblen and Hamblin are the only ones dealing exclusively with the use of the drug by mouth.

There have been a number of other reports on the use of sodium amytal in obstetrics, but these concern themselves chiefly with the intramuscular, intravenous, or rectal administration of the drug.

Our object was to determine the proper dose of sodium amytal by mouth that would give good analgesia. We used the drug in 100 cases in active labor. Our criterion for the proper time for the administration of the drug was the activity of labor rather than the degree of cervical dilatation. Most of the cases, however, were about two fingers dilated at the time the drug was given. The initial dose varied from 3 to 15 grains. In our 3-grain series, 3 patients had more than one dose. In the 9-grain group, one patient received an additional 6 grains, while in the 12-grain group, 5 received an additional 6 grains each.

At first the drug was administered in capsule form followed by a small amount of water. It was observed, however, that if the drug were taken on an empty stomach, the patient would often go into a deep sleep within

\*Read at a meeting of the Brooklyn Gynecological Society, October 2, 1931.



a few minutes, but if it were taken with a small amount of food, the effect was not so abrupt. Within ten minutes the patient was quite drowsy and within fifteen to thirty minutes a good many of the women would go into a deep sleep. This was particularly true when the larger doses were used. In the average case the patient would rest quietly between pains. With a pain, the patient would moan, toss about, and in some instances become markedly restless, often sufficient to require restraint. There was no apparent change in pulse or respirations in any of the cases.

In our series of cases there was no appreciable analgesia unless the larger doses were used. Our results seem to contradict those obtained by Morehead and Mussey and agree with those of Hamblen and Hamblin.

Of our 100 cases, 37 had good or fair analgesia during labor. Only 4 of these successful cases were given small doses of the drug (3-6 grains), while the remaining 33 received larger doses (9-15 grains). Of the cases that received 15 grains each, 66 per cent had good analgesia. All of these cases required some ether at the time of delivery, although the amount used was considerably less than usual.

A good number of patients went into a deep sleep lasting from three to twelve hours after delivery. Catheterization during labor was necessary much more frequently than is usually the case. It was difficult to make patients who had received sodium amytal take fluids, both during labor and for some time after delivery.

Amnesia, like analgesia, is obtained only with the use of the larger doses. Of 65 patients who received from 3 to 9 grains of the drug, only 2 had amnesia. Of 35 who received from 12 to 15 grains of sodium amytal, 15 or 42.8 per cent had good amnesia.

A study of the method of delivery shows that 36 patients were delivered by forceps and one by version. Twenty-one of these forceps cases and the version were done for teaching purposes. Of the remaining 15 forceps deliveries, 3 or 4 may be attributed to the use of the drug. The restlessness, lack of cooperation, and inability to make use of the pains after full dilatation, made forceps delivery necessary in these cases.

With the use of the smaller doses, restlessness was not an important factor. As the dosage increased however, the number of patients who became unruly increased. Of 51 patients receiving from 9 to 15 grains of sodium amytal, 17 were restless. In other words 1 out of every 3 was sufficiently restless or unruly to require restraint. Some of these patients would toss about in bed; a number of them assumed the crouching position; several were observed placing the hand in the vagina, and a few even fell out of bed in spite of the use of side boards. Three patients became distinctly maniacal, requiring the use of restraints and morphine. A good many of the patients were entirely uncooperative when on the delivery table. They would squirm, toss about, disarrange the sterile drapings, and refuse to bear down with pains.

There were no ill effects on the baby when the smaller doses were used. Of 51 cases in which the initial dose was from 9 to 15 grains, 11 babies were narcotized at birth. These babies breathed spontaneously but did not cry at once. A few of the babies, however, had shallow and irregular respirations at birth. Slight external stimulation or the use of a little carbon dioxide was all that was necessary to make them breathe properly and cry. Several of the babies, although breathing regularly and crying when stimulated, remained drowsy for an hour or more. Most of the babies nursed well when put to the breast, even those who showed some degree of narcosis at birth. Of the 11 narcotized babies 6 were delivered by forceps and 5 spontaneously.

In the entire series there were 2 stillbirths.

The first stillbirth occurred in a para v. The membranes had ruptured before admission and there was meconium stained amniotic fluid. There was uncertainty as to the presence or absence of the fetal heart. When the labor became active, 6 grains of sodium amytal were given. The patient became maniacal and had to be morphinized. She was delivered of a stillbirth by low forceps. It is our opinion that the use of the sodium amytal was not responsible for the stillbirth.

The second stillbirth occurred in a primigravida. When she was in active labor and the cervix three and a half fingers dilated, she was given 12 grains of sodium amytal. At this time the fetal heart was not heard. Membranes were ruptured artificially and only a small amount of thick greenish amniotic fluid escaped. The patient delivered herself spontaneously of a stillborn fetus followed by only 2 or 3 ounces of thick greenish amniotic fluid. Autopsy was negative except for pulmonary atelectasis. Gross and microscopic studies of the placenta were also negative. This case was considered one of oligohydramnios.

In the series of 100 cases, 53 showed moderate or good relaxation of the soft parts. In 3- and 6-grain groups only 28.5 per cent showed relaxation, whereas in the larger dosage groups 76.5 per cent showed good relaxation. It is our impression that this relaxation reduced the number of perineal lacerations.

Sodium amytal did not increase the incidence of postpartum hemorrhage, nor did it seem to prolong labor.

#### CONCLUSIONS

Our experience with sodium amytal has been rather disappointing. It is true that in a large proportion of cases, large doses of the drug will give satisfactory analgesia, amnesia, and relaxation of soft parts. However, these advantages are greatly outweighed by the frequent occurrence of marked restlessness, an increase in the number of instrumental deliveries, and frequently narcotized babies.

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(For discussion, see page 155.)

# ADENOCARCINOMA OF THE CERVIX IN A TWENTY-TWO MONTHS' OLD CHILD\*

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**M**ALIGNANCY of the female genital tract in childhood is generally sarcomatous in nature, the vaginal form of sarcoma botryoides and sarcoma of the ovary being the lesions most frequently encountered (Lynch,<sup>1</sup> McFarland,<sup>2</sup> Scheffey<sup>3</sup>). Carcinomatous lesions of the tract, on the other hand, are comparatively rare, both in children and young women.

Carcinoma, originating in or confined to the cervix in childhood, is the most infrequent lesion of all, and before the age of ten is a pathologic curiosity. Bonner,<sup>4</sup> Morse,<sup>5</sup> and Baldwin<sup>6</sup> have recently published comprehensive articles in regard to carcinoma of the female genital tract in childhood, exclusive of the ovary, thoroughly reviewing the literature on the subject.

Prior to the case herewith reported, but three authenticated cases of carcinoma of the cervix have been recorded as occurring in children ten years of age or younger. They are: (1) Glockner's patient,<sup>7</sup> aged seven, diagnosed adenocarcinoma by R. Meyer and Ruge; (2) Ganghofner's patient,<sup>8</sup> aged eight, pronounced adenocarcinoma by Chiari (both reported by Mergelsberg<sup>9</sup> also); (3) Morse<sup>5</sup> and McDonald's patient,<sup>10</sup> aged ten, whose lesion was regarded by Ewing and Smith as "a very cellular adenocarcinoma with notable embryonic characteristics."

Reference has been made by Frank<sup>11</sup> to an adenocarcinoma reported by Bumm,<sup>12</sup> Aschheim<sup>13</sup> and Berktañ,<sup>14</sup> as occurring in a six or seven months' old infant, but as this was evidently a vaginal neoplasm, it should not be recorded as a cervical lesion. This patient is probably the same one observed by Palmer Findley in the Charité Frauenklinik, and mentioned in personal communications to Frank and the authors. Recently Kohlhaas<sup>15</sup> reported a malignant tumor of the cervix in an infant of sixteen months, but the histologic picture did not permit of its classification as a cervical carcinoma.

## CASE REPORT

The patient was a twenty-two months' old infant, referred by Dr. Walter Livingston, of Landsdowne, Pa., and was admitted to the Gynecological Service of Dr. Brooke M. Anspach, Jefferson Medical College Hospital, on July 6, 1931, because of slight and intermittent vaginal bleeding of four weeks' duration, unaccompanied by pain. Prior to this disturbance the child appeared to be healthy and normal in every respect.

\*Read at a meeting of the Obstetrical Society of Philadelphia, November 5, 1931.

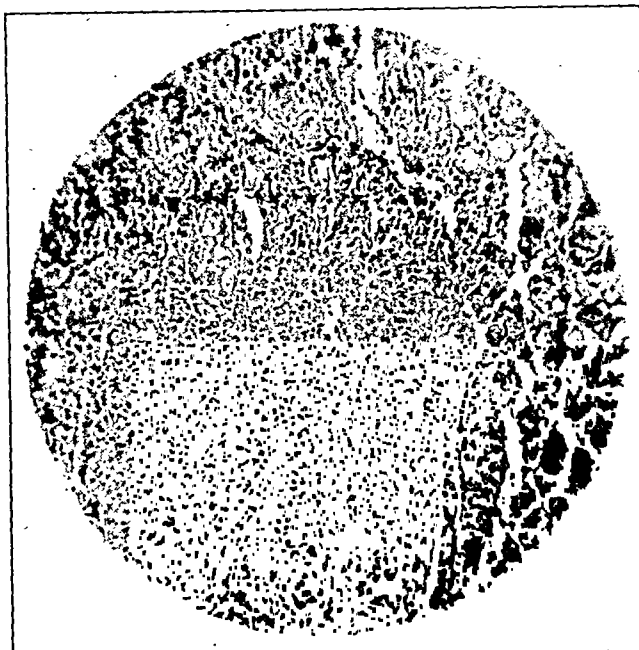


Fig. 1.—Biopsy from cervix (low power). The solid mass of undifferentiated tumor cells occupy the center of the microphotograph. A few small spaces lined by columnar cells can be recognized.



Fig. 2.—Biopsy from cervix (high power). With this magnification the columnar epithelium lining some of the spaces can be definitely identified.

General physical examination negative. Complete blood studies revealed a moderate secondary anemia. Wassermann and Kahn tests were negative. The external genitalia were normally formed, and no evidence of trauma was found. No masses or enlargements could be palpated in the abdomen and glandular adenopathy was absent. X-ray studies of the chest revealed no abnormality.

Upon rectal examination, a mass continuous with the fundus of the uterus could be palpated through the rectovaginal septum. Under gas anesthesia, employing the knee-chest position, direct inspection of the vagina and cervical area was accomplished by means of a Kelly cystoscope. This procedure caused profuse bleeding, but vaginal irrigation cleared the field sufficiently to observe a friable, fungus-like growth occupying the cervical area, and encroaching on the vaginal vault. A portion of this tissue was removed for biopsy, and the vagina lightly packed. The histologic report by Dr. B. L. Crawford is as follows:

"Examination of sections from the biopsy specimen reveals that it is composed largely of granulation tissue in which there is extensive inflammatory reaction and necrosis, especially on the surface, with a framework of connective tissue containing numerous small blood vessels. Toward the center of the specimen there is a small area composed of very cellular structure which is evidently neoplastic in character. The tumor cells are undifferentiated and are rather large, with large deeply stained nuclei, many of which are undergoing mitosis. These cells for the most part have no characteristic arrangement, forming solid clumps with a small amount of fibrous tissue stroma, but some of the cells can be recognized as columnar epithelial cells and form indefinite acini. No normal structure is observed. Many sections were examined from various levels of the small pieces of tissue and all are similar."

While the greater portion of the tissue is inflammatory and necrotic, there is sufficiently well preserved tissue in a small area near the center of the specimen, which can be definitely identified as malignant tumor tissue, and is considered to be of epithelial origin, and columnar in type, rather than squamous cell.

*Diagnosis.*—Adenocarcinoma of the cervix. (Figs. 1 and 2.)

#### TREATMENT

Because of the inaccessibility of the lesion, a course of deep x-ray therapy was decided upon, being employed intensively over a period of five to six weeks. It was planned to apply radium subsequently. During this time gradual failure in health occurred, the child developing diarrhea, progressive anemia, an antipathy for nourishment, vomiting and bronchial irritation. Repeated intraperitoneal blood transfusions were administered, but the infant became progressively weaker and death occurred on August 26, 1931.

#### AUTOPSY REPORT

The autopsy (limited to examination of the abdomen) was performed three and one-half hours postmortem by C. J. Bucher: No evidence of malformation of the body is observed. The peritoneal cavity contains a small amount of clotted blood, but no evidence of inflammation of the peritoneum is observed. The pelvic organs are free from adhesions and were removed in toto. The ovaries and tubes are normal. The fundus of the uterus is small and the cavity is normal. The cervix is enlarged and thickened. On section, the cervical tissue is found to be soft and the mucous membrane of the portio and canal is replaced by necrotic, grayish tissue which is soft and friable on the surface, and rather firm and of a yellowish color in its deeper portion. One portion of the cervix is thicker than the other and is nodular in appearance. The mucous membrane of the vagina is somewhat congested but no evidence of ulceration or other lesion is observed. No enlarged lymph nodes either in the pelvis or abdomen could be demonstrated. The other abdominal organs

appear normal except the colon. The mucous membrane of the entire colon is inflamed and ulcerated from the cecum to the anus. The ulcers are irregular, superficial, and have rather ragged margins.

Histologic examination of sections from the cervix are rather disappointing as there is such extensive necrosis of the tissue, probably due to the irradiation. Many sections were examined from different areas of the cervix, but no evidence of neoplastic tissue, such as that observed in the biopsy sections, could be demonstrated. In the deeper portions of the cervical tissue, small collections of epithelial cells forming indefinite acini, are observed, which strongly suggest carcinomatous infiltration, but this is not conclusive. No histologic evidence of neoplastic involvement of the other organs is observed. (Fig. 3.)

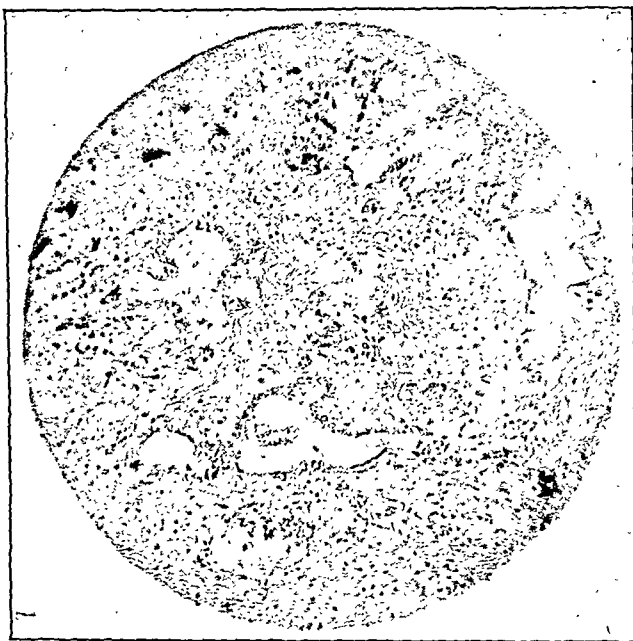


Fig. 3.—Section from cervix removed at autopsy (low power). The extensive degeneration and necrosis of the tissue is evident. The small spaces lined by epithelium and the presence of clumps of cells in the deeper portions of the cervix, are suggestive of carcinoma, but inconclusive.

#### COMMENT

While no hemorrhage occurred following the initial vaginal examination, an intermittent blood streaked discharge was observed, that sometimes had a foul odor. No further vaginal inspections were made during the course of the x-ray treatment. Postmortem revealed that the lesion was limited to the cervix and apparently arrested, marked necrosis being present. No evidence of local extension or metastasis, gross or microscopic, supported this belief. In our opinion the resultant toxemia from the ulcerative colitis was the actual cause of death, irritation of the colon by the x-ray exposures having first initiated a catarrhal colitis with diarrhea that progressed rapidly to the ulcerative state.

Microscopic sections from the biopsy specimen were examined by Drs. Brooke M. Anspach, Thomas S. Cullen, Howard A. Kelly, Emil Novak, Curtis Burnham, James Ewing, Robert T. Frank and Virgil H. Moon, all of whom concurred in the histologic

diagnosis of adenocarcinoma of the cervix. We are very grateful for their interest and comments on this case and take the liberty of quoting from several of the written reports, as follows:

Dr. James Ewing, New York: "The section of tumor of the cervix in an infant shows undoubtedly a carcinoma. I think it is essentially a papillary adenocarcinoma arising from the glands and probably from some embryonal defect in the structure of the cervix. It is the earliest case that I have seen. Autopsy material does not permit any diagnosis."

Dr. Robert T. Frank, New York: "From the biopsy specimen, no other diagnosis but that of adenocarcinoma is possible. These conditions, of course, are extremely rare, and in the majority of instances, where it was possible to obtain sufficient material, it was found in some areas a mixed tumor was present. From the autopsy specimen no additional information is obtained, except that a tremendous necrosis of tissue occurred after the radiation."

Dr. Emil Novak, Baltimore: "I agree with Dr. Crawford's report. The anaplasia and undifferentiation of the cells is so definite, that, from a pathological standpoint, the diagnosis of malignancy seems compelling, even though the amount of tissue available for study is so small. Were such a section obtained from an adult woman, it would undoubtedly be pronounced malignant. Coming, as it did, from an infant, one must always think of the possibility of some unusual embryological condition which might simulate cancer, but no such explanation occurs to me in this instance. From the rather definite acinous tendency in some areas of the section, it would seem that the growth is probably of the adenocarcinomatous type. Pathological diagnosis: Adenocarcinoma of the cervix."

#### SUMMARY

1. We herewith present a case of adenocarcinoma of the cervix in a twenty-two months' old child, terminating fatally.

2. The histologic diagnosis has been concurred in by the above mentioned group of gynecologists and pathologists.

3. From a survey of the literature, we believe it to be the earliest case on record of an adenocarcinoma originating in or limited to the cervix uteri.

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SAMPSON: PELVIC ENDOMETRIOSIS AND TUBAL FIMBRIAE



Fig. 36.



Fig. 37.



Fig. 38.

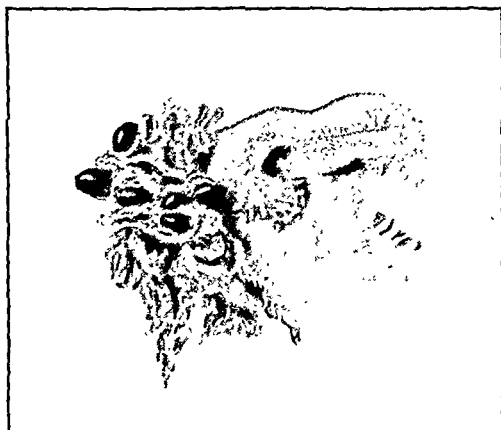


Fig. 39.

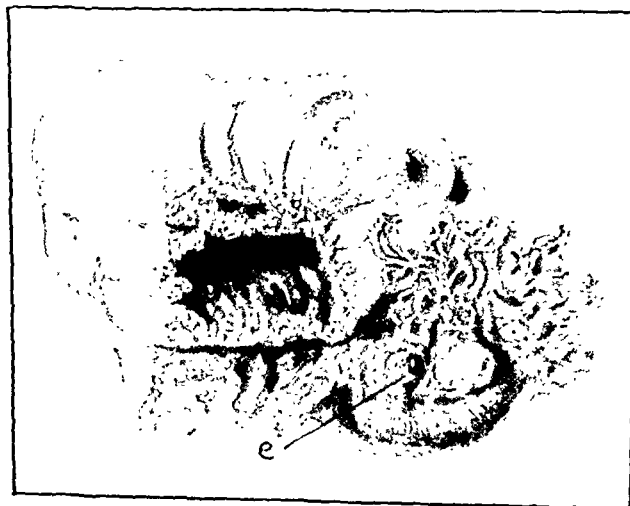


Fig. 40.

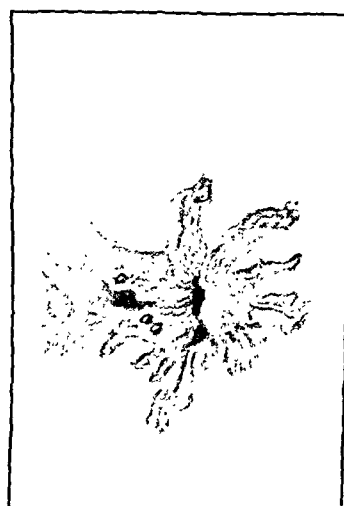


Fig. 41.





## A STUDY OF THE PREDISPOSING CAUSES OF BREAST ABSCESS

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STATISTICS concerning suppurative mastitis, or abscess of the breast are rare. One who consults the standard obstetric textbooks, hoping to learn how often he may expect to encounter this condition in his practice, is disappointed. This is due to the fact that most textbooks are based on hospital experience, while abscess of the breast seems to belong almost exclusively to private practice. To gain a more definite knowledge of some of the factors in the etiology of breast abscess H. W. Johnson, R. A. Johnston, and I began five years ago to study these cases a little more closely. During that time we have found 43 instances of suppurative mastitis which required incision and drainage. This paper is an analysis of those cases.

That abscess of the breast is a disease of private practice has already been mentioned. This is clearly demonstrated by comparing the incidence reported by an average hospital with that reported by individuals. In the five years prior to September 1, 1931, the Houston Baptist Hospital had 5,245 obstetric patients, with only 7 breast abscesses. This gives the remarkably low incidence of 0.13 per cent. For the same period we have detailed records of 2,522 patients, 43 of whom developed abscess of the breast. This places our incidence at 1 in 58, or 1.7 per cent. These figures indicate that statistics obtained from institutional records give a false picture of the frequency of breast abscess. They further remind one that the condition is fairly common.

The likelihood of a patient having a breast abscess depends largely upon how many babies she has nursed previously. If she is nursing her second baby, her chances of avoiding breast complications are greatly increased, and with her third or later babies she is practically immune to them. Of the 43 cases, 30 or 70 per cent developed in women nursing the first baby. The second baby accounted for 10 more, with the third, fourth, and ninth babies responsible for one each. These are the findings one would expect, for an organ should be better prepared to do a task or resist an infection each succeeding time it is called upon to do so. The last three patients mentioned, the para iii, the para iv, and the para ix, each had an added predisposing factor. The para iii was a member of that group with red hair, which seems to offer little resistance to breast infections. The para iv was a very unclean woman who also had an offensive pyorrhea, and the para ix had two excellent foci of infection in an active pyelitis and an acutely inflamed Bartholin's gland. Had these added factors not been present, I believe those women would have been safe. Multiparity, then, seems to be a safeguard against breast abscess.

On the other hand, one abscess does not predispose to another. Three patients whose breasts required incision have since successfully nursed a subsequent baby.

The length of time that elapsed before these abscesses developed varied considerably. The earliest ones appeared during the second week post-partum, while the latest one appeared in the sixteenth week. The greatest number occurred during the fourth week. However, the average was five and one-half weeks. This is a puzzling finding. The greatest number of cracks and fissures of the nipple are found in the first week that nursing is established and are rare after the tenth day, and we have been taught that these are the gateways through which bacteria enter the breast. One would expect, then, to find the greatest number of abscesses in the second week. It is unlikely that the bacteria would enter the breast in the first ten days and then lie dormant for several weeks before becoming active. One suggestion that immediately offers itself is that the organism enters the breast through the blood stream rather than through the fissures. Other facts supporting this will be pointed out later.

There is a definite seasonal variation in the incidence of breast abscess. If the year is divided into two periods of six months each, starting May 1 and November 1, it is found that only 12 of the infections appeared in the first period, while 31 occurred during the six months from November through April. This six months fall and winter period coincides with the time when the general health of people is poorest, and when infections of all kinds are most common. It reminds one again of the bloodborne infection theory. The month showing the greatest number of abscesses (8) was November, 1929, and during that time Houston was suffering an epidemic of influenza.

The weight of the baby at birth has some bearing on breast infections. Textbooks give the average birth weight as 7 pounds, 2 ounces. Our average baby weighs slightly more. The baby whose mother develops an abscess of the breast, though, averages 8 pounds at birth. On the theory that the larger and more vigorous baby could do more damage to the nipple than could the smaller baby, one would expect the larger infant's nursing to be more often following by infection, and this is quite true.

Abscess of the breast is essentially a disease of the well-to-do. Most of these 43 patients are cultured, clean, and have servants. Their husbands are professional men. Why they should have more breast infections than their socially less fortunate sisters is difficult of understanding. Yet in a fairly large charity practice at Jefferson Davis Hospital and Florence Crittenden Home I have never encountered an abscessed breast. DeLee, in discussing puerperal infection, says that "it is more common among the delicately bred well-to-do than among the poor, who, through ages of squalor and filth, have developed immunities, which the others

in their protected lives, do not possess." That statement seems to be equally applicable to abscess of the breast.

It was formerly thought that there was little likelihood of a breast becoming abscessed unless its nipple was fissured or inverted or otherwise badly formed. Yet in only three of these cases was there any gross abnormality of the nipple. That deformities appear so infrequently in this series, is due to our practice of abolishing nursing permanently with the first signs of even a simple mastitis in a breast bearing a deformed nipple. I believe this plan has forestalled many abscesses.

Unfortunately, it has not been practical to determine by laboratory examination the type of infecting organism in this series. Clinically the staphylococcus group seems to have been responsible for about three-fourths of the abscesses, with the colon bacillus and others present in the other fourth. Whether these bacteria all entered the breast through the nipple, I am not prepared to say, but it is significant that foci of infection were present in 20 patients, or almost half of the series. One immediately becomes suspicious that some of the bacteria might have been carried into the breast by the blood stream. The kidney pelvis was the most frequently found focus, with the tonsils, the teeth, and the sinuses appearing less often.

In 9 patients a history of trauma was obtained. Two of these allowed the baby thirty minute nursing periods after all nursing had been forbidden. In the other 7, massage was the traumatic agent. Any attempt to reduce the incidence of abscessed breasts must include teaching nurses not to massage an engorged, painful breast.

Abscess of the breast has its origin in a simple mastitis. Whether or not it goes on to abscess formation depends largely on the treatment given the mastitis. The most successful plan we have followed includes the prohibition of nursing and pumping, the application of ice bags, and the avoidance of all manipulation. The ideal treatment should probably include both breasts. About 20 per cent of our patients develop a mastitis of sufficient severity to warrant this treatment. That only 1.7 per cent proceed to abscess formation is evidence of its soundness.

Prenatal attention to the breasts and nipples does not seem to affect their career of lactation one way or the other. No benefit comes of massaging the breast with oils. About 20 per cent of our patients were given a mixture of glycerite of tannin, compound spirits of lavender, and water to use on the nipples during pregnancy. Five of them later developed abscess of the breast, among them being some of the most virulent of the series.

The type of nipple antiseptic used has little influence on the formation of breast abscesses. A few years ago, I was convinced that a modified Dakin's solution applied to the nipple before and after nursing would prevent many breast complications. Further study has disproved this.

The Dakin's solution was used on 55 per cent of our patients, and they developed 58 per cent of the abscesses. Boric acid is of little value as an antiseptic, and the Dakin's solution used was no better. I believe sterile water would be equally as good.

Blonde patients are far more likely to develop abscess of the breast than are brunettes. The breast being of ectodermic origin, this agrees with the experience of dermatologists, who find that the pyodermic infections are less common in brunettes. The darker skin seems to offer more resistance to staphylococci invasion. In this series there were 28 blondes to 15 brunettes, almost two to one. Of the 28 blondes four had red hair. This group is one that we have learned to watch closely. Very few women with red hair go through lactation without breast complications arising.

Several other factors which may influence the formation of breast abscess have been studied but the knowledge gained has not been sufficient to warrant discussion of them. Operative delivery does not seem to be a factor. A high percentage of these patients show allergic reactions. Exposure of the breast to sunlight during the prenatal period may be a valuable prophylactic measure. These and other questions will be given further study.

In conclusion, several definite statements may be made about abscess of the breast. It is a condition fairly common in an individual obstetric practice. It is a disease of the primipara and of the blonde. It is two and one-half times as common in fall and winter as in spring and summer. The average abscess occurs during the baby's sixth week, and the baby is overweight. It is more common among the well-to-do, and it does not depend on deformities of the nipple. Foci of infection and trauma seem to play a part in it. There is some evidence that the infection is carried to the breast by the blood stream.

1620 MEDICAL ARTS BUILDING.

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**Schultze-Rhonhof: Conservative Treatment of Pulmonary Tuberculosis in Pregnancy.** *Ztschr. f. Geburtsh. u. Gynäk.* 96: 17, 1929.

The author gives the following reasons why tuberculous women should not become pregnant: The possibility of making worse the pulmonary process cannot be absolutely excluded. The increase in the size of the family and the raising of another child augments both the demands on the mother and often financial embarrassment with its attendant harmful results. These factors influence unfavorably the subsequent course of the tuberculosis. If mother and child are not separated, the latter runs the chance of an early postnatal infection. If they are separated, the mother suffers mentally from loss of her child, which has a harmful effect on the course of the tuberculosis.

LESTER E. FRANKENTHAL, JR.

## LABOR IN THE ELDERLY PRIMIPARA\*

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A FIRST pregnancy and labor in a woman well advanced in years is always regarded as a hazard both by the laity and by the profession. Yet, this interesting and important subject has received very little attention in our vast obstetric literature. In this country only four references are found on the subject, while the French, German, and Scandinavian journals contain quite a number of articles. Most of the articles take the age of thirty as the boundary line between a young and a so-called elderly primipara; very few concern themselves exclusively with the truly old primipara, the woman near forty or over. O. Linden, in 1929, studied the labors in 202 women over forty years of age while V. Esmann, in 1930, reviewed the labors of 75 primiparae between forty and forty-six years of age.

In this article we have chosen thirty-eight years as a more or less arbitrary age limit but with certain reservations in mind. First, the course of labor in women from thirty to thirty-seven or thirty-eight differs very little in most respects from that in women under thirty. The tables in J. P. Freeland's article bring this point out very strikingly. Secondly, the primipara of thirty-eight or over, as well as her attending obstetrician, has a perfect right to consider this first pregnancy as possibly the last one. Thirdly, it is in this advanced age group that we would naturally expect to find an increased number of uterine inertias with long labors, toxemias, resistant soft parts, and the resulting increase in fetal and maternal morbidity and mortality.

While it is true that a certain number of old primiparae encounter a good deal of difficulty during their labor and delivery, the comparative ease and rapidity with which some of these women go through labor indicate clearly that age is only one of several factors involved. Not infrequently the other factors concerned are far more important than the patient's advanced age. We shall endeavor to prove this particular point as we present a study of our cases.

In 1912, Kate C. Spain reviewed and studied the European literature on the subject. She decided that the dangers often associated both by the laity and the profession with childbirth in elderly primiparae were greatly exaggerated; that cervical rigidity, when present, was almost always due to uterine inertia, and that eclampsia was not more frequent as it was supposed to be. She did find, however, that boys were more common than girls and that twins were a trifle more frequent.

Leopold Meyer, Jaroschka and Remmelts believe that the difficult labors in some of these cases are a question of constitution rather than one of age. Some of these women marry late because of definite physical defects, others conceive late because

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\*Read at a meeting of the Brooklyn Gynecological Society, October 2, 1931.

of genital hypoplasia; and these are the cases that tend to have uterine inertias with long difficult labors.

#### STUDY OF CASES

*Age.*—From 1914 to 1931 there were delivered at our hospital, 48 primiparae between the ages of thirty-eight and forty-four; of these, 32 or two-thirds of the total, were under forty, while 16 or one-third were forty or over.

*Length of Time Married.*—This fact was recorded in only 18 instances. There were 9 patients who had been married from one to five years; 8 were delivered vaginally and one by cesarean section. The remaining nine had been married over five years; of these only 5 were delivered vaginally and 4 by cesarean section. A study of the cases in this group suggests the fact that the longer the woman is married before she becomes pregnant, the greater the chance for a long and difficult labor and operative interference. Some of these women are probably the "constitutionally inferior" type mentioned by Leopold Meyer, Jaroschka, and Remmelts.

*Condition of Membranes and Duration of Labor.*—The average duration of labor (excluding the cases that were sectioned) was twenty-two and a half hours. In those cases where membranes were intact, the average duration of labor was twenty-one and eight-tenths hours, while in those with ruptured membranes it was twenty-eight and one-tenth hours. The shortest labor was seven hours, the longest seventy-two hours. From these figures it is apparent that in this series of cases, the labor was a little prolonged, and where the membranes were ruptured, labor lasted seven hours longer than when membranes were intact. In Margaret Schulze's 337 cases over thirty years of age, the average duration of labor was only sixteen and a half hours, and ruptured membranes did not seem to prolong labor. Quigley, in a similar series of 307 cases, reports labor as not prolonged. Possibly the greater duration of labor in our series is to be explained by the fact that we are dealing with a group of older women.

TABLE I. METHOD OF DELIVERY

Cases delivered vaginally	37 or 77%
Cases delivered by cesarean section	11 or 23%
The vaginal deliveries: Spontaneous	17 or 46%
Low Forceps	13
Median Forceps	5
High Forceps	2
	} or 54.0%

Over three-fourths of all the cases were delivered per vaginam, while less than one-fourth were delivered by cesarean section. A little less than half (46 per cent) of the vaginal deliveries were spontaneous, while the remainder (54 per cent) were delivered by forceps. There were two high forceps in this series and both resulted in stillbirths. These two were the only stillbirths in the entire series, an incidence of 4.1 per cent.

Two of the patients delivered by median forceps had a bilateral Dührsen's incision of the cervix.

Eleven cases, or 23 per cent of the total number, were delivered by cesarean section. Ten of these were classical and one a Porro. In no case was a cesarean done merely because of the advanced age of the patient. In every single instance there were one or more additional and important indications, such as toxemia, contracted pelvis, fibroids, disproportion, abnormal presentation, etc. Nine of the 11 patients had a test of labor lasting anywhere from six to eighteen hours. Two were elective sections. The Porro section was an elective procedure performed on a gravida iv, para o, forty-two years of age, married five years, and giving a history of 3 previous miscarriages. Patient was admitted to the hospital at full term, not in labor, with a transverse presentation and multiple fibroids. She made an uneventful recovery. Eight of the sections were done under gas-oxygen or ether, while 3 were done under spinal anesthesia with neocaine.

All of the babies lived. Two of the mothers died; one of postoperative lobar pneumonia and the other of a general peritonitis.

A glance at Table II will show the indications for cesarean section in each case and the length of time the patient was in labor before section was performed. This table also brings out the fact previously mentioned that in every case delivered by cesarean section, there were factors involved which were more important than the patient's advanced age per se.

TABLE II.

CASE	INDICATIONS FOR SECTION	TEST OF LABOR
1	Disproportion, previous myomectomy	8 hours
2	Toxemia, flat pelvis, fibroids	none, elective
3	Disproportion, funnel pelvis	18 hours
4	Disproportion	18 hours
5	Disproportion, contr. outlet, toxemia	12 hours
6	Disproportion, fibroids (multiple)	12 hours
7	Dystocia due to lower uterine segment, fibroid	12 hours
8	Fibroid, toxemia, contr. pelvis	10 hours
9	Disproportion, previous myomectomy	6 hours
10	Transverse presentation, multiple fibroids	None, Porro, elective
11	Toxemia, 1° uterine inertia	12 hours

A comparative study of the duration of labor and method of delivery in the cases under forty years and in those of forty and over, reveals the following:

First, the average duration of labor in the older group is nineteen and



one-tenth hours against twenty-four and three-tenths hours for the younger group.

Second, spontaneous deliveries occurred in 50 per cent of the younger group against 25 per cent in the older group.

Third, forceps deliveries and cesarean sections are considerably more frequent in the older group.

Table III brings out these points and also compares the method of delivery in our patients of forty and over and the 75 cases reported by V. Esmann in 1930.

TABLE III

	THIRTY-EIGHT TO FORTY YEARS 32 CASES	FORTY AND OVER 16 CASES	FORTY AND OVER 75 CASES (V. ESMANN)
Duration of labor	24.3 hours	19.1 hours	?
Spontaneous deliveries	50 %	25 %	49.3%
Forceps	31.2%	43.7%	40 %
Cesarean section	18.7%	31.2%	1.3%

There were 5 cases of preeclamptic toxemia in this series. None of them was very severe. There were no cases of eclampsia although it is said to be more common in old than in young primiparae. Three of the 5 were delivered by classical section, 1 by low forceps, and in one, labor was induced by the introduction of a Voorhees bag. This patient delivered spontaneously. All the babies and mothers lived. The incidence of 5 toxemias in 48 cases or 10.4 per cent is a rather high figure, but we are dealing with a group of women well advanced in years, and that may be the possible explanation. V. Esmann reports 13 cases of albuminuria and 4 of eclampsia in 75 primiparae of forty and over, giving a higher incidence, a little over 22 per cent.

There were 6 cases of contracted pelvis in this series, an incidence of 12.5 per cent. Two were simple flat, 2 funnel, and 2 patients had contracted outlets. Schulze reports 8.6 per cent contracted pelvis, Jaroschka 8.3 per cent, and Quigley 11 per cent. Of our 6 cases, 4 patients were delivered by cesarean section, 1 by low forceps, and 1 by median forceps following bilateral Dührssen's incisions of the cervix.

Five cases had no laceration, 7 had a first degree laceration, and 7 had a second degree laceration. Eighteen mediolateral episiotomies were performed. There were no third degree perineal lacerations. There was one rectovaginal fistula and two lacerated cervixes. Both of these followed bilateral Dührssen's incisions of the cervix. The case of rectovaginal fistula warrants a few words. The patient, a primipara of thirty-nine, was delivered by low forceps following a right mediolateral episiotomy after she had been in labor for eighteen hours. The cervix had been fully dilated and the head on the perineum for one hour.

There was no extension of the episiotomy and the perineum was repaired immediately by placing several layers of interrupted sutures. The puerperium was uneventful up to the ninth day when it was discovered that the patient was passing small amounts of feces per vaginum. Examination revealed a small rectovaginal fistula. The only possible explanation for the fistula is that one of the deep sutures buckled a small portion of the rectal mucosa. Suture necrosis followed and the fistula resulted. A secondary repair was done twelve days postpartum, but was unsuccessful. About one month postpartum the patient was readmitted to the hospital and the sphincter ani was incised, making a complete perineal laceration out of the rectovaginal fistula. This was done in order to avoid a periproctitis and the patient was to come back for a complete perineorrhaphy six months later.

*Morbidity.*—Under this heading we are including cases that not only ran a temperature but also cases that had true obstetric complications even though the temperature was normal. To include patients with real pathologic conditions it seems to us, is more important than limiting the morbidity to cases that merely run a postpartum temperature. To be specific, a postpartum hemorrhage or a rectovaginal fistula, with or without temperature, is more truly an obstetric morbidity than a cesarean section which has a reaction temperature for the first two or three days postpartum.

In this series, there were 13 morbidities, an incidence of 27 per cent.

TABLE IV. MORBIDITIES

Moderate postpartum hemorrhage	3 cases
Lochiometra	3 cases
Sepsis with pelvic thrombophlebitis	1 case
Phlebitis of superficial veins	2 cases
Rectovaginal fistula	1 case
Cholecystitis and secondary anemia	1 case
Four-day temperature following section	1 case
Two-day temperature following a forceps delivery	1 case
	13 cases

*Mortality.*—In this group of 48 cases, 2 mothers died. Both of these were postoperative deaths following classical cesarean section. One patient died of lobar pneumonia on the sixth day postoperative, while the other one died of a general peritonitis on the fifth day postoperative. The peritonitis death was confirmed by autopsy.

*The Babies.*—Of the 48 babies, 46 were born alive and 2 were stillborn, giving a fetal mortality of 4.1 per cent. Linden reports a fetal mortality of 10.2 per cent, V. Esmann 9.3 per cent, Freeland 8.2 per cent, Schulze 7 per cent, and Quigley 5 per cent.

Both stillbirths followed the use of high forceps which were done a good many years ago, one in 1916 and one in 1921. The 46 babies born alive were all discharged from the hospital. Of these 1 had clubbed

feet and double harelip, 1 had pemphigus and recovered, and 1 had hemorrhagic disease of the newborn and recovered.

The sex was recorded in 44 cases; there were 24 females and 20 males. The weight was recorded in 43 cases. The average weight was exactly seven pounds.

#### SUMMARY

In our series of 48 cases, 13 had a morbidity, 2 mothers died, and 2 babies were stillborn. Over three-fourths of the patients were delivered per vaginam while 23 per cent were delivered by cesarean section. The patients who were forty years old and over had a shorter average labor than those under forty, but more of them had to be delivered by forceps or cesarean section.

#### CONCLUSIONS

1. The dangers and difficulties often associated with labor in the old primipara seem to be exaggerated. Age is only one of several factors involved.

2. Contracted pelvises are more common in old primiparae than in younger ones.

3. Toxemia is also more common.

4. The average duration of labor is longer by several hours.

5. The constitution of the old primipara, especially the one that gives a history of a long period of sterility, seems to bear a definite relationship to the type of labor and delivery.

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876 EASTERN PARKWAY.

(For discussion, see page 155.)

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Halloran, Chris R.: Syphilis and Pregnancy. Am. J. Syph. **14**: 222, 1930.

Although pregnancy does not apparently decrease susceptibility to infection with *Treponema pallidum*, the defense mechanism of pregnancy alters the clinical manifestations of syphilis in such a way that primary and secondary lesions are frequently either absent or very mild. Although the Wassermann reaction in pregnancy cannot be relied upon with the same degree of assurance as in the non-pregnant, a strongly positive blood Wassermann verified on repetition is diagnostic of syphilis. The blood Wassermann of the infant of the syphilitic woman is not reliable for the first month of life. The serologically and clinically normal child of a syphilitic mother must be kept under close observation and placed upon anti-syphilitic treatment immediately should definite evidence of the disease become manifest. The pregnant woman tolerates a modified form of antisyphilitic treatment well, though the same unusual results are occasionally encountered as in treatment of the nonpregnant.

C. O. MALAND.

# REPORT OF AN UNUSUAL CASE OF LEIOMYOSARCOMA OCCURRING IN THE URINARY BLADDER

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**L**EIOMYOSARCOMA apparently is one of the rarest types of neoplasm. Three cases only are reported as involving the urinary tract. Such growths appear most frequently in the uterus, where 9 instances have been noted in the body and 1 in the cervix. There are 1 case in which the growth was primary in the stomach, 2 in the jejunum, and 1 secondary in the liver, the origin of which was undetermined.

This survey was made early in 1931. Since that time Dr. Samuel R. Meaker has reported 4 cases of leiomyosarcoma of the uterus, 1 of which was a true myoma malignum. (AM. J. OBST. & GYN. 22: 400, 1931.) Leiomyosarcoma of the pleura is reported by L. Catron in the *Archives of Pathology*, 2: 847-863, 1931, and a primary leiomyoplastic sarcoma of the skin by W. Newmann, in *Centralbl. f. allg. Path. u. path. Anat.* 52: 65, July 20, 1931.

So rare is this form of smooth muscle sarcoma that many authorities make no mention of it in their works. A great many tumors of doubtful origin are reported, however, in which the observers fail accurately to designate the pathologic type. There seems to be some difficulty in classifying this form of tumor. A growth may show unstriped muscle fibers, with large, deeply staining nuclei and other typical features, and yet not merit the designation of true leiomyosarcoma.

SARCOMAS OF THE BLADDER  
Classified According to Their Microscopic Diagnoses

	ALBARRAN	CONCETTI	DARLING	DENING	GERAGHTY	GARDNER	LENORMANT	MUNWES	MINTER	WATSON	TOTAL
Round cell	21	20			1			30			72
Ruso cell	7	7									14
Mixed cell	4	4						8			16
Lymphosarcoma	3	3		2		1		4			13
Alveolarsarcoma	3	3						6			12
Fibrosarcoma	4	4						5	1		14
Myxosarcoma	1	1		2				7			11
Giant cell sarcoma	1	1						2			4
Telangiectatic sarcoma	1	1						2			4
Chondrosarcoma	1	1						2			4
Spindle cell sarcoma					1			16			17
Myosarcoma	2	2						5			9
Epitheliosarcoma							1				1
Not stated	7		8	7		6		7		2	37
											228

Meigs states that the frequency of myosarcoma is problematical, his own opinion being that it constitutes from  $\frac{1}{2}$  to 1 per cent of all sarcomas. In 1926, Cecil published the accompanying table, listing 228 sarcomas of the bladder, of which 9 were myosarcomas. While 13 different types of sarcoma are here reported by ten leading authorities, to whose work references are made throughout the literature, there is no mention of leiomyosarcoma.

The purpose of the present paper is to add one more case to the records of leiomyosarcoma of the urinary bladder. In this case there is a history of dysuria and frequency of two years' duration *without the classical symptom of macroscopic or microscopic blood in the urine*. There was no appreciable loss of weight or strength. The growth of the tumor mass was sudden and rapid. When the patient came for examination, it was impossible to introduce a cystoscope because of the almost complete obliteration of the bladder cavity. These unusual clinical features, in addition to the comparative rarity of the pathologic findings, and the ease with which the tumor could be removed, present a picture of bladder neoplasm which appears to be unique.

R. L., white, female, aged sixty years, was admitted to the Gynecological Department of the Jewish Memorial Hospital on May 16, 1929. She complained of frequency of urination, loss of weight, and a gradual increase in the size of her abdomen. Family history irrelevant.

Patient had one child living, twenty-five years of age. Ten years ago a laparotomy was done at St. Luke's Hospital for fibroid uterus. Panhysterectomy was supposedly done, although the record of this operation is incomplete.

For the past two years the patient has complained of frequency of urination, voiding sometimes as often as every fifteen minutes. This symptom has become so aggravated in the past month that she has had little control of her bladder. During the past six weeks she has noticed a gradual enlargement of the abdomen, some loss of weight, general lassitude, and backache. No vaginal discharge. Bowels regular. She has never to her knowledge passed either blood or bloody urine. There is considerable abdominal pain of constant, dull, aching character.

Abdominal examination showed the liver to be of normal size, with no point of tenderness or massing above the line of the umbilicus. Reaching to the umbilicus, situated in the midline down to and below the symphysis pubis was a semisolid oval-shaped mass about 5 inches in width.

Vaginal bimanual examination revealed no cervical stump. The tumor was easily reached through the vaginal culdesac, and filled the entire true pelvis.

Catheterization of the bladder with a solid catheter was impossible due to inability to introduce it. The soft catheter obtained a few drops of clear urine. No cystoscopy could be done.

A preoperative diagnosis was made of abdominopelvic tumor probably of ovarian or parovarian origin, impinging on the bladder and reducing its capacity.

Urinalysis of the catheterized specimen showed some turbidity; albumin 2 plus; no sugar, acetone or diacetic acid; many white blood cells; no red blood cells. Blood chemistry showed no unusual features.

*Operation.*—Midline incision was made over the tumor extending from the symphysis pubis to the umbilicus, through skin and fascia. This brought the anterior surface of the mass into the wound without entering the peritoneal cavity.

The tumor evidently was extraperitoneal and probably of bladder origin. Careful dissection at the lower portion showed on either side the entering ureters, thus confirming the belief that the tumor involved the bladder.

The anterior bladder wall was incised its whole length, the lower end of the incision being above the entrance points of the ureters. The wall was about three-

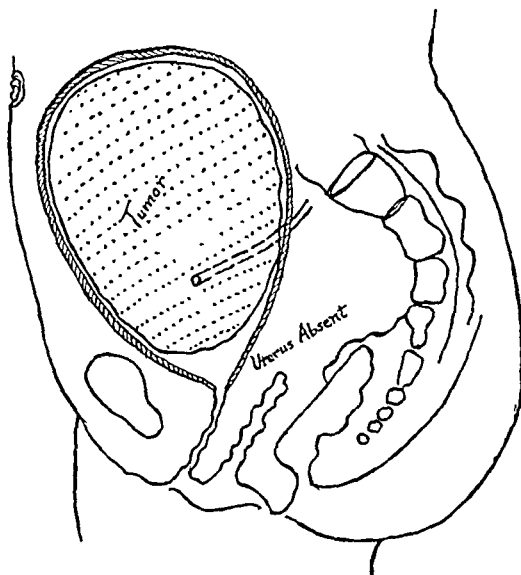


Fig. 1.—Showing intravesical position of tumor.

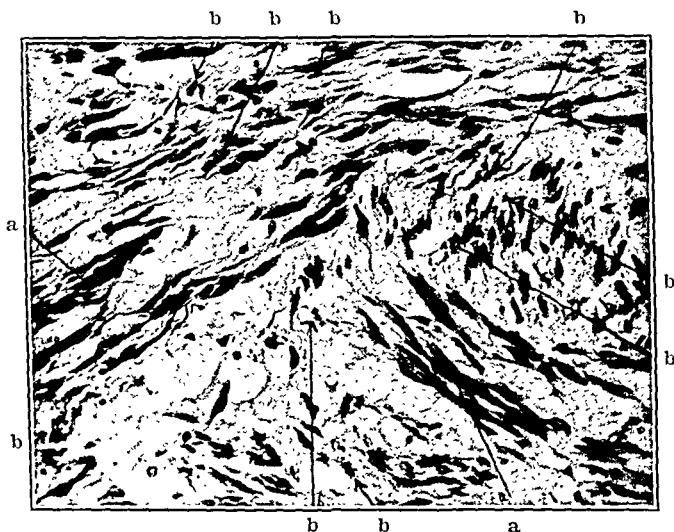


Fig. 2.—High power of tumor section showing intertwining smooth muscle fibers and mitotic figures.

quarters of an inch thick. The line of demarcation between the bladder wall and the tumor was now quite distinct, with the posterior portion of the tumor definitely encapsulated and taking up almost entirely this immensely distended bladder cavity.

Free dissection of this mass was then easily accomplished, with very little or no bleeding; as this musculocystic tumor was thoroughly encapsulated.

A Marion tube was left in and held by linen sutures.

The postoperative course was quite uneventful until the thirty-third day after operation, when there was a sudden suppression of urine, with convulsive seizures. On the thirty-sixth day postoperative, there was a sudden rise in temperature to 104.8° F., with convulsion and death.

*Pathologic Report.*—The flat, slightly oval-shaped tumor, white-brown in color, was about 18 cm. long, 9.5 cm. wide, and 3.6 cm. thick. Weight 420 grams. Surface was irregular, with some superficial and deeper notches and elevations. The cut surface showed the tumor consisting of a homogeneous mass, mottled in appearance. The brown colored parts were fleshy and soft. The white colored parts were soft and resembled degenerated tissue. There were signs of capsule formation.

*Microscopic.*—There were many smooth muscle fibers, some well developed and others fairly well developed, with nuclei oval-shaped or oblong; few empty capillaries. Many muscle fibers showed hyaline and mucoid degeneration, with numerous mitotic figures in various stages of mitosis. The number of mitotic figures varied between 8 and 30 to 40 per field. Occasionally there were a few connective tissue fibers visible.

*Diagnosis.*—Leiomyosarcoma of the bladder.

As this tumor resembled an ovarian or parovarian tumor, it fell into the hands of a gynecologist. Since we had not received a single report of leiomyosarcoma of the uterus or ovaries in some 500 hysterectomies and cophorectomies, the question arose why so many muscle-bearing tumors had in no instance undergone this form of malignant change. Therefore, an extensive search was undertaken, which disclosed the extreme rarity of such tumors, only 18 cases having been recorded in either American, English, or Canadian literature.\*

The specimen here described was submitted to several of the leading pathologists in New York, some of whom were uncertain as to its exact nature, but most of them eventually agreed that it was a leiomyosarcoma, and probably the largest of its kind they had ever seen. A careful search was required in order to make certain that all portions of the tumor were infiltrated with sarcoma cells and cell nests, thereby thoroughly establishing its pathologic status. In other words, many of the muscle fibers, besides showing hyaline and mucoid degeneration, showed many mitotic figures in various stages of mitosis, sometimes as many as 30 or 40 to the field, an unusually large number as compared with the cases previously reported.

#### SUMMARY

1. Leiomyosarcoma is one of the rarest types of tumor. The case here presented makes the nineteenth on record in English literature. It is notable for its great size, its rapid growth, its perfect encapsulation, and the absence of classical symptoms.

2. A review of the reported cases of leiomyosarcoma discloses the finding that the great majority of these tumors are of uterine origin.

\*The current German, French, and Italian literature yield one case each—of the stomach, the uterus, and the female genitals respectively. Due to uncertainty as to foreign nomenclature and diagnostic criteria, these cases have not been abstracted. For lack of space, it is not possible to publish the extended review of the literature.

3. The histologic criteria for this type of malignancy are indefinite. It is hoped that an effort may be made to standardize the classification of nonepithelial tumors.

4. As with carcinoma, metastases are a late symptom; when this stage is reached, the case has usually become hopeless. The only safeguard lies in periodical examinations and the early recognition of malignancy or potential malignancy.

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## PREGNANCY IN ONE HORN OF A BICORNATE UTERUS FOLLOWING EXTIRPATION OF THE OTHER HORN\*

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*(From the Clinic of the Woman's Hospital)*

MRS. S. R., a healthy appearing, well developed, German, thirty-two years of age, first came under my care at the Woman's Hospital for the treatment of an incomplete abortion of a four months' pregnancy. The uterus was curetted, and she made an uneventful recovery. It was decided that the abortion was due to a congenital malformation of the uterus.

Fifteen months prior to admission, she had been operated upon at the Frauenklinik at München, for a fibroid tumor and removal of a "second womb" as she described it. Within the first twenty-four hours after this operation the abdomen was reopened to control a postoperative hemorrhage. A subsequent communication from Professor Doederlein, stated that at the time of operation she had a bicornate uterus with a rudimentary left horn and a fibroid in the right horn the size of "an English walnut." At operation he had removed the left tube and ovary as well as the rudimentary horn. In other words she still had the right tube and ovary and the ovum which was being expelled had developed in the remaining right horn from which a fibroid had been removed.

The patient had been married eleven years and was extremely anxious for a child. She had failed to conceive during the first four years of married life but at the time of this admission was aborting for the fifth time in seven years. She had aborted once at six weeks, twice at two months, once at three months and now at the time of this admission was aborting for the fifth time at the fourth month of pregnancy. She had aborted three times before having the laparotomy described above and this was the second abortion since her operation.

The patient was one of eight children. Her mother and sisters had all had difficult confinements. Her mother and one sister had been delivered by cesarean section.

Her past medical history was negative except that she had had scarlet fever as a child. Her menstrual periods began at fifteen years, and were always regular with a good flow for four days every month. The periods had always been painful and accompanied by nausea and vomiting.

The general physical examination was essentially negative except for a moderate secondary anemia. R.B.C. 3,920,000. Hemoglobin 64 per cent. The blood Wassermann and urine were negative. Systolic blood pressure was 140 mm.

Pelvic examination revealed normal pelvic measurements, and normal appearing external genitalia, vagina and cervix. The uterus was enlarged, soft and drawn to the right. The remaining appendage seemed normal to palpation.

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\*Read at a meeting of the Section of Obstetrics and Gynecology, New York Academy of Medicine, November 24, 1931.



In view of the history of five pregnancies, none of which had progressed farther than four months, probability of going to term seemed rather doubtful. However, the patient was extremely anxious for a child and was advised to report for observation at once when another pregnancy started.

Five months later she conceived, her sixth pregnancy.

While she was skipping every one of her first seven menstrual periods she had definite, very painful, uterine cramps and scant vaginal bleeding. She remained in bed during the time that her periods were being skipped and was given full doses of morphine and codeine to relieve the pain and to stop uterine contractions.

Although the outlook seemed rather hopeless throughout, she finally reached full term and was delivered of a normal female child weighing 6 pounds 2 ounces, by

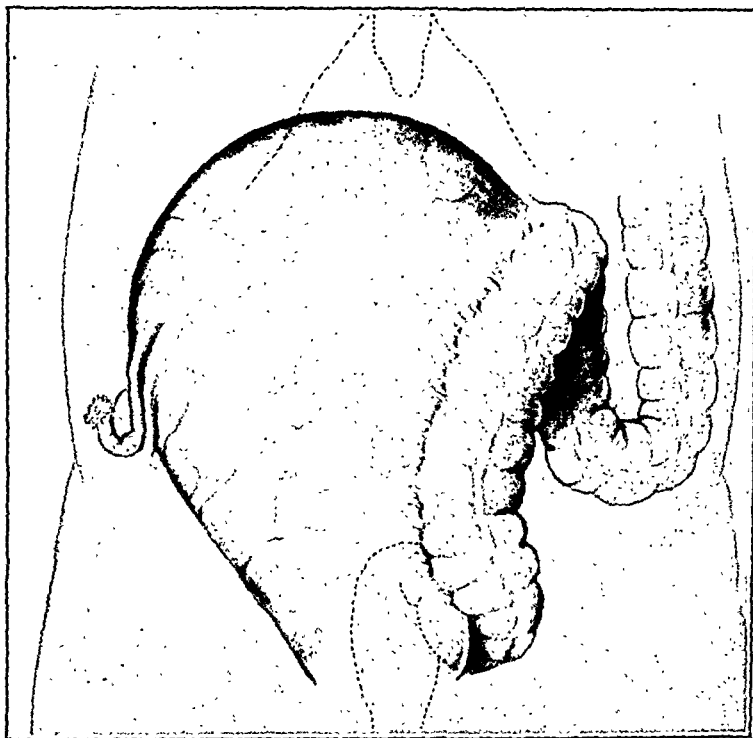


Fig. 1.—Pregnant right uterine horn with sigmoid firmly attached over area from which left horn had been removed. Note attenuated myomectomy scar in anterior uterine wall.

classical cesarean section soon after labor began, as the cervix was long, firm, and undilated. It seemed that at least an average labor was to be expected and that there was considerable danger of a rupture of the uterus. The attenuated scar of the previous myomectomy could be distinctly seen and the entire uterine wall was unusually thin. The fact that the patient had had so many pregnancies without a living child was also a factor.

A loop of sigmoid was adherent over the entire area from which the left rudimentary horn of the uterus had been removed. It was not kinked and appeared to be functioning normally. No effort to free it was made.

The patient made an uneventful recovery; the abdominal wound healed by primary union and the mother and child were discharged in good condition sixteen days after operation.

Notwithstanding that the patient had been advised to avoid another pregnancy for at least two years, she became pregnant again when her first child was but four months of age. Thirteen months after the first cesarean she was practically at

term again. The patient was more comfortable during the second pregnancy until the last month when she suffered from sharp pains over the uterus. Throughout this pregnancy the baby seemed too small for the period of gestation.

The patient was admitted to the hospital for observation two weeks before term because pains over the uterus had become unusually severe. Soon after admission an enema was given and uterine contractions began at once and were accompanied by very sharp abdominal pains so intense that the patient held her abdomen with her hands.

Rupture of the uterus was feared. An anesthetic was given as soon as possible and the abdomen was opened. A spontaneous rupture of the uterus was found in the anterior wall through the combined scars of the previous myomectomy and

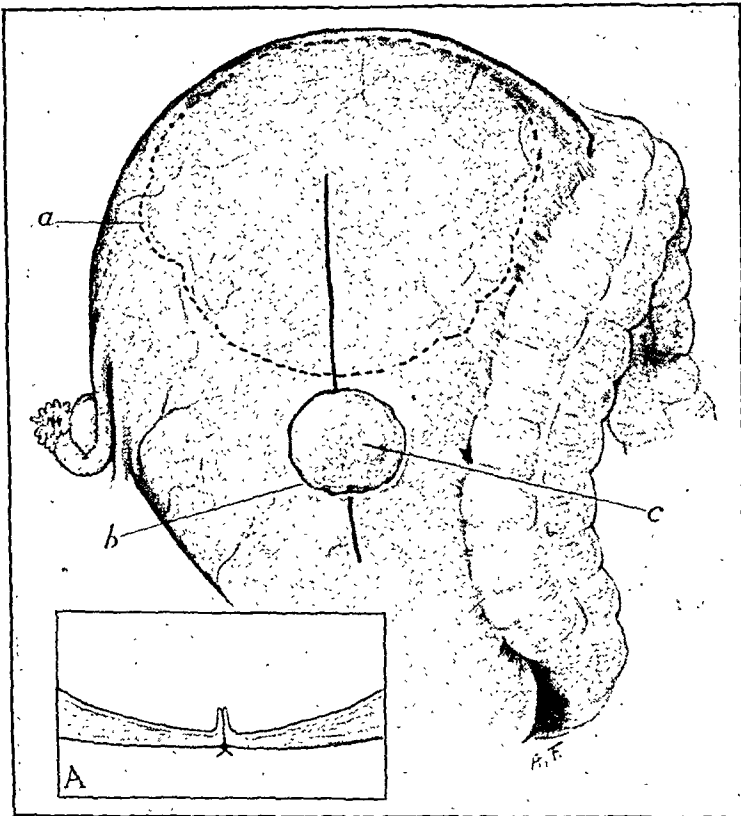


Fig. 2.—Pregnant right uterine horn as observed at time of second cesarean section with rupture (*b*) in anterior wall, and protruding fetal sac (*c*). Approximate location of placenta is given by (*a*). Insert (*A*) shows method of closure of thin anterior uterine wall.

cesarean section. There was no blood in the peritoneal cavity. The opening in the uterus was about 4 cm. in diameter and the membranes of the fetal sac were bulging through the aperture. The opening was enlarged and a female child weighing 5 pounds 8 ounces was removed. The baby cried as soon as delivered but seemed to have very little vitality and died about four hours after birth. In the meantime the baby was seen by a pediatrician who declared it to be a typical asthenic child. About one-half of the placenta was attached over the very thin anterior wall and the blood supply was poor over this area. This might easily account for poor development of the baby.

The uterine wall was so thin that it was necessary to denude the peritoneum and infold the edges in order to effect a firm closure. The patient was then sterilized.

She again made an uneventful recovery. At her last follow-up examination, one year after the last operation, she was in good health, pelvic examination showed nothing abnormal, and her menstrual periods were regular and normal.

This case demonstrates a very desirable result from the original conservative gynecologic operative procedure. It emphasizes the necessity for careful observation during pregnancy of certain patients who have congenital uterine malformations and demonstrates how perfect cooperation on the part of the patient during pregnancy may influence the result.

33 EAST SIXTY-EIGHTH STREET.

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## REPORT OF A CASE OF TRIOVULAR TRIPLETS\*

ALBERT H. ALDRIDGE, M.D., F.A.C.S., NEW YORK, N. Y.

*(From the Clinic of the Woman's Hospital)*

MRS. S., an Irish-American female twenty-five years of age, in her third pregnancy. She had had one previous normal full-term spontaneous delivery, of an eight and one-half pound baby after six hours of labor, at twenty-two years of age, and a spontaneous abortion at two months' gestation one year later. From her first delivery there was a laceration of the pelvic floor, moderate relaxation of the vaginal walls and a bilateral laceration of the cervix. The mother of the patient was a twin. General physical examination negative. Her menstrual periods were always normal, 5 days' duration. At the time that she applied for treatment the uterus seemed definitely too large for the period of gestation as shown by her menstrual history. Dating the onset of her pregnancy from one week after the first day of her last period she could not have been more than nineteen weeks pregnant. However the uterus was enlarged to at least the size of a pregnancy of twenty-four weeks' duration. A fetal heart could not be heard and the patient had not felt life. The possibility of an existing multiple pregnancy, hydatidiform mole or hydramnios, was considered.

At the time that she skipped her first period she had slight cramplike pelvic pains and had spotted for two days. It was thought that this was due to an early threatened abortion.

The patient was kept under careful observation. She soon began to feel life, and a fetal heart could be heard. The pregnancy appeared to be progressing in a normal way, except that the uterus always seemed too large for the period of gestation, and the patient suffered more than usual from heartburn, nausea, and constipation.

As pregnancy advanced the patient's abdomen became so large that she was almost incapacitated. It was decided to admit her to the hospital for observation, as it seemed that the pregnancy might have to be terminated. At this time she was at most thirty-seven weeks pregnant; the cervix was about 2 cm. dilated; a breech presented, and a fetal heart could be heard faintly over each upper quadrant. Two fetal hearts of different rates could not be definitely made out. The abdomen was enormous in size, and abdominal palpation was made difficult by what seemed to be an excessive amount of amniotic fluid.

An x-ray examination showed that the great distention of the uterus was due to triplets, all three of which were presenting as breeches.

Two days after admission the membranes of one fetal sac ruptured spontaneously; a large amount of fluid was expelled; the patient immediately went into very active labor, and spontaneously delivered the first baby, under light ether anesthesia, in

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\*Read at a meeting of the New York Obstetrical Society, November 10, 1931.

exactly two hours. The two remaining sacs were then artificially ruptured and the other two babies were easily delivered.

After delivery of the third baby the mother developed what seemed to be a paroxysmal tachycardia. Although she showed no signs of shock and her condition was not at any time alarming the pulse rate suddenly became about 200 per minute. After twenty-five minutes the pulse suddenly dropped to 80 per minute, and continued at that rate. In spite of the extreme distension of the uterus, labor was un-

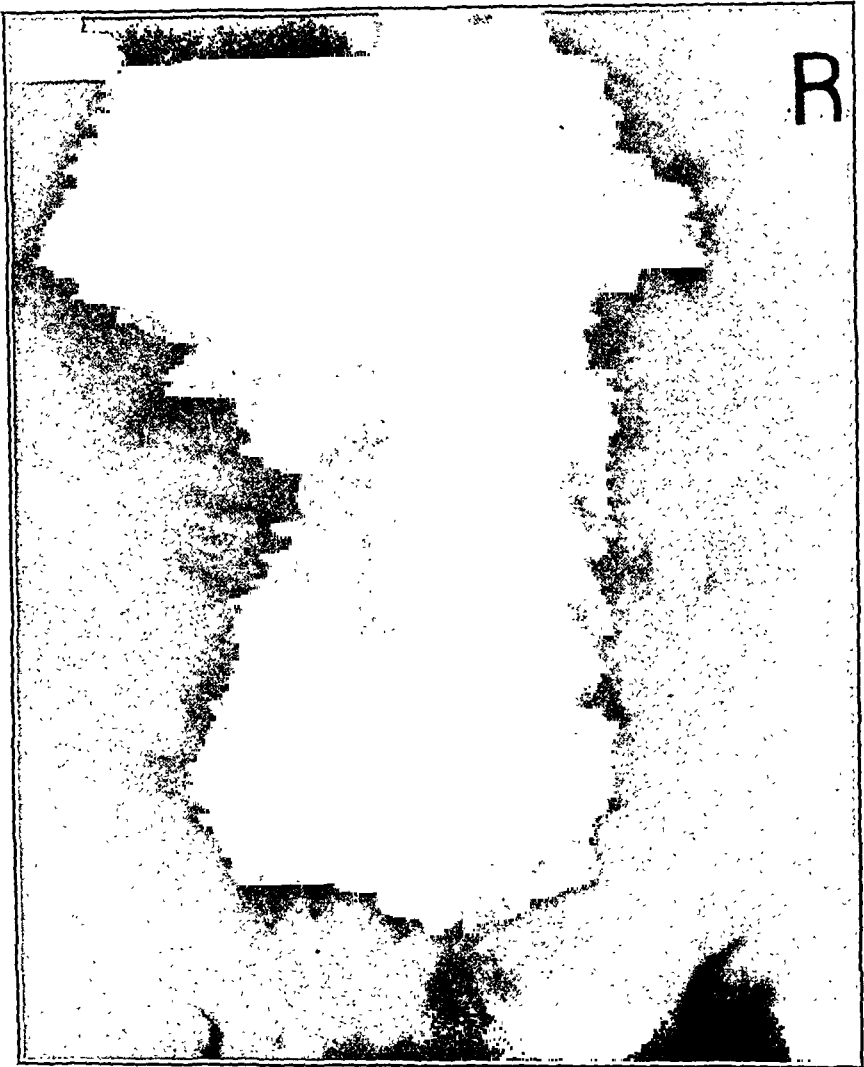


Fig. 1.—X-ray showing triplets, all three presenting as breeches.

usually vigorous and loss of blood was only moderate. The mother's postpartum course was uneventful.

All three babies were males, and weighed respectively: 4 pounds 7 ounces, 4 pounds 3 ounces, and 3 pounds 3½ ounces. The placentas were delivered without difficulty. There were three distinct placentas and fetal sacs. Each sac had both an amnion and chorion. In other words the triplets which had been delivered were triovular.

All three babies did well after birth. The two larger ones were discharged when thirty-one days old, weighing 5 pounds, 9 ounces, and 5 pounds, 6 ounces, respectively.

The third baby was discharged when forty-one days old weighing 5 pounds, 13 ounces. Unfortunately the largest and oldest of the three developed a severe gastroenteritis and died when four months of age. The other two have thrived.

The case is of interest because it emphasizes again the value of the x-ray as an aid to diagnosis in certain obscure cases near term.

33 EAST SIXTY-EIGHTH STREET.

## AN IMPROVED UTERINE DILATOR

WILLIAM D. FULLERTON, M.D., F.A.C.S., CLEVELAND, OHIO

**D**ILATATION of the cervix is a very common surgical procedure for which many instruments have been devised. This fact alone indicates that there is no absolutely satisfactory instrument. Probably the best and the one most commonly used is some form of slightly curved solid cylinder in graded sizes, such as the Hegar. But this has a very serious defect, which we have, by our modification, entirely eliminated.

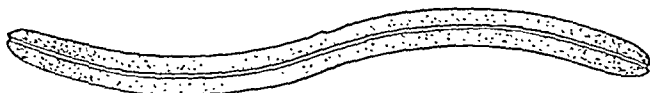


Fig. 1.—Hegar-Fullerton uterine dilator, showing lumen throughout its length to eliminate piston action in uterus.

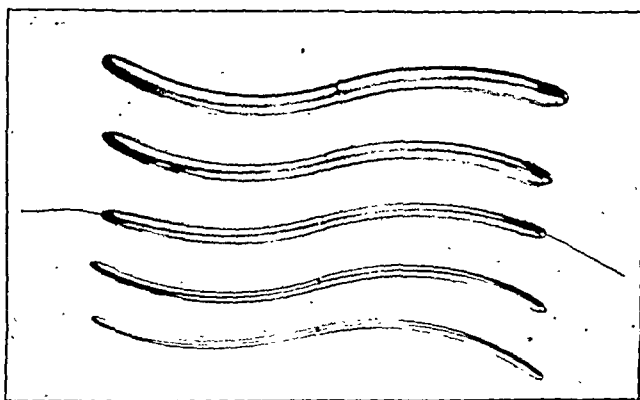


Fig. 2.—Set of 5 Hegar-Fullerton uterine dilators, 5 to 14 mm. in diameter, with stylette through lumen of center dilator.

The uterine cavity is frequently frankly infected, especially in cases of incomplete abortion or malignancy of either cervix or fundus. When a sound or the first small dilator is introduced through the cervix and carried up into the uterine canal, there is always some traumatization of the endometrium with resulting desquamation of epithelium and a certain amount of bleeding. As the successively larger dilators are introduced through the tight cervix the traumatism is increased, and there is a perfectly typical and mechanical piston action, making of the uterus an anatomic syringe barrel and forcing the contents into the tubes and even out into the pelvic cavity. This is easily verified when the abdomen is opened following a curettage, and a varying amount of free blood will often be found in the culdesac or can easily be milked from the fimbriated end of the tube.

It can readily be seen how malignant cells may in this way be carried into the tubes or peritoneal cavity where transplantation may occur. Infection will also be carried upward, and this fact may account for many cases of the extension of the infectious process where removal of retained secundines is done following abortion. The same mechanics may add an etiologic factor in some cases of endometriosis.

The modification which we have made of the Hegar dilator entirely eliminates these undesirable possibilities. This has been accomplished by making a tubular lumen through the center and length of the dilator, Fig. 1. The lumen is 1 mm. in diameter and permits the passage of a heavy wire stylette to keep the lumen clean and free of obstruction. The dilators are made in graded sizes from 3 to 16 mm. in diameter, and are 20 cm. long. A set of 5, ranging from 5 to 14 mm. in diameter, Fig. 2, are found sufficient and practical.

When these dilators are used, there can be no increased pressure within the uterine canal, and the air, blood and desquamated uterine epithelium is freely discharged through the lumen.

I wish to express my thanks to the J. F. Hartz Co., of Cleveland, who were painstaking in the experimental manufacture of this instrument, and from whom they may now be obtained, listed as the Hegar-Fullerton uterine dilator.

1622 KEITH BUILDING.

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## A MODIFIED ADHESIVE DRESSING

JACOB MUNTER LOBSENZ, M.D., NEW YORK, N. Y.

THE first wound inspection after a laparotomy is often feared by the patient and a nuisance to the surgeon, due to the firm attachment of the adhesive plaster to the dressings and skin beneath.

To inspect the wound, it is necessary either (1) to tear off the entire adhesive dressing, or else (2) to cut through the center line of the dressing, pull back the lateral flaps along with the adherent dressing beneath and then to change the dressing cut holes through the edges of the adhesive, run tape through and then tie across in the manner of Montgomery strips.

The latter method is the preferred one, but the effort of loosening the adhesive from the dressings beneath, so as to be able to pass a scissors through, is time-consuming and often causes an uncomfortable pressure and pulling to which the patient objects. The scissors generally cut the dressings in addition to the adhesive plaster.

During the last twenty years I have been using a method of applying adhesives which the patients have appreciated, and which apparently seems to be new to many surgeons and nurses who have seen and admired it, and whose enthusiasm has prompted me to describe the method. This dressing is not original with me but was observed by me years ago; however, I have been unable to trace its inventor.

The usual method of strapping an abdominal or other flat surface wound is to apply the dressing and then to run the adhesive strips across directly on the dressing and to anchor the adhesive on the skin beyond the lateral edges of the dressing.

In the simple, convenient modification of using adhesive, dressings are applied as usual. Then a strip of adhesive about three inches in width and long enough to extend three inches above and three inches below the upper and lower borders of the dressing, is applied first; longitudinally, adhesive side up, and canvas side against the dressing. This strip simply rests on the center line of the dressing. Then the transverse adhesive strips are applied as usual, making contact with the adhesive side of the longitudinal strip. The loose adhesive ends of the longitudinal strip at the

upper and lower borders of the dressing are now turned over on the transverse adhesive strips and the dressing is complete.

There is now a longitudinal canal in the center of the dressing mapped out by the turned over upper and lower ends of the first adhesive strip, to which no dressings are adherent beneath. To cut down the dressing, it is then very easy to pass a bandage scissors upward along this canal and to cut the adhesive plaster in half. The two lateral flaps are easily turned aside to their attachment to the skin, and dressings changed.

To refasten the dressing we have two lateral flaps whose mesial edges have two layers of adhesive through which corresponding holes are cut, tape is passed through the holes in these reinforced edges, either for lacing or tying; and we now have

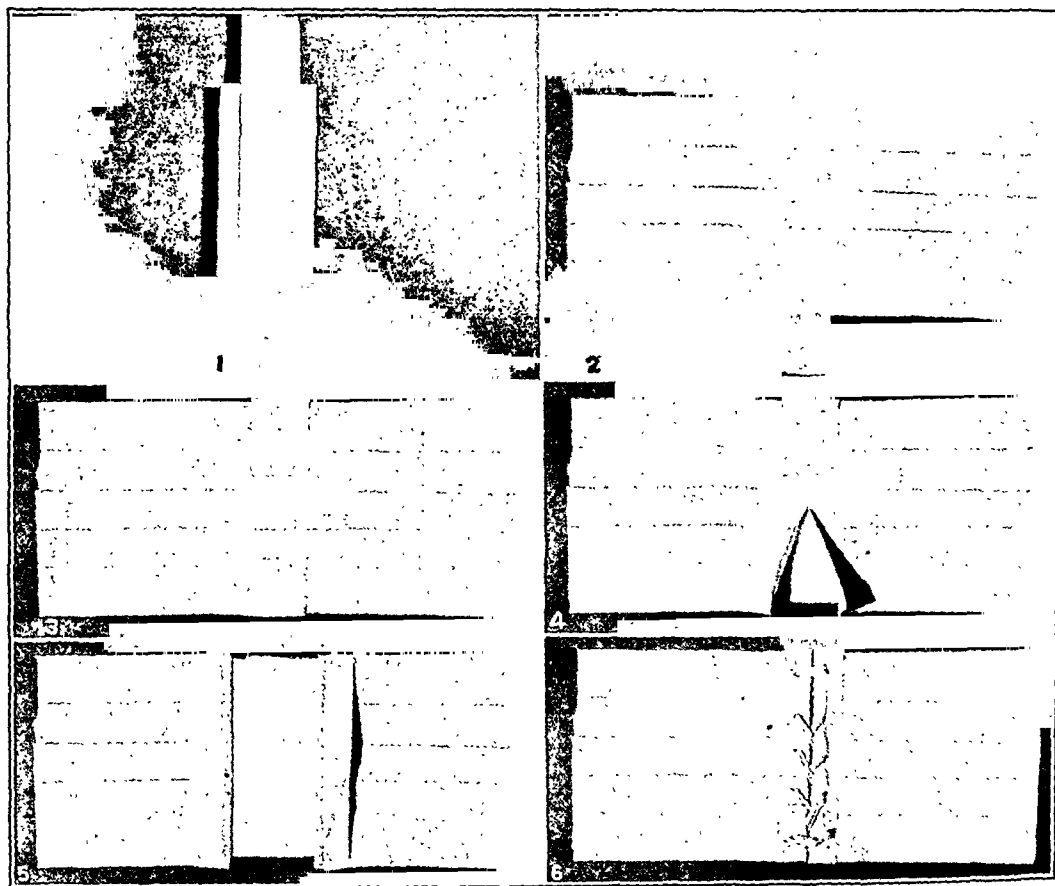


Fig. 1.—Adhesive strip extending above and below the dressing, adhesive side up.

Fig. 2.—Cross strips holding dressing in place.

Fig. 3.—Dressing completed with upper and lower ends of first strip turned over.

Fig. 4.—Longitudinal canal in center of dressing partly cut through.

Fig. 5.—Longitudinal canal completely cut through, showing reenforced edges and dressing free from adhesive.

Fig. 6.—Dressing again held in place by the original adhesive in a modified form of Montgomery strips by lacing the two large flaps.

Montgomery strips in the shape of two large adhesive flaps.

This method of applying adhesive allows easy and frequent inspection of the wound without the tearing off of the original adhesive applied in the operating room; and in the majority of cases requires only one application of adhesive during the patient's entire stay in the hospital.

# Society Transactions

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## NEW YORK OBSTETRICAL SOCIETY

MEETING OF NOVEMBER 10, 1931

DR. A. H. ALDRIDGE reported a case of **Trioovular Triplets**. (For original article see page 140.)

DRS. A. W. BINGHAM AND H. W. TITUS reported similar cases of triplets diagnosed with x-rays.

DR. S. A. WOLFE (by invitation) presented a paper entitled **End-Results After Excision of the Cervix Interpreted from Pathologic Findings**. (For original article see page 87.)

### DISCUSSION

DR. C. A. GORDON.—Dr. Wolfe has shown us that the largest percentage of cures is in the low infection group. It is quite possible that in that same group just as high a percentage, or even a better figure, might be obtained by the use of ordinary office procedures, such as the cautery.

I believe that we should look critically at the cervix before definitely deciding to operate upon it. Although there is a definite place for the cautery, for the Sturmdorf operation, and for amputation of the cervix, yet we might not always succeed in picking out the right procedure in the individual case.

The lesson is, I think, that the possibilities for office procedures should be extended and, according to this presentation, it seems to me that the chances for operative success are fraught with so much danger that the cautery has an increased importance as compared with operative procedures.

DR. ELIOT BISHOP.—There is one form of treatment of the cervix that Dr. Wolfe has neglected in his treatise, namely, the cautery amputation of the cervix. Coming from a locality where Byrne, Skene, and Dickinson did their work, we think in terms of the cautery.

Its use is not applicable to a patient who will keep on menstruating, as a cicatrix may form that will produce not only stenosis but real atresia of the cervix, with resultant hematometra and its train of pathology.

In a woman beyond the menopause, or in one who is being treated for benign bleeding or suspected carcinoma with radium, so as to produce the menopause, the cautery gives the most nearly perfect results. It does not look so well, at the time, as an instrumental amputation, but the result in a few weeks is so good that the uninstructed can hardly believe that it has been done with a cautery. In a patient who shows by biopsy examination that carcinoma exists, we feel more contented with this procedure, knowing that we have not opened up any lymphatics.

If radium has been used coincidentally with this cautery amputation, we must admit that healing is slower with a discharge for three or four weeks, but healing does take place in the end, with equal satisfaction. It makes us feel that the patient has the least chance in the world to develop cancer.

DR. F. W. SOVAK.—I had the privilege of reporting a pre- and postoperative study of 250 consecutive cases to this Society a few years ago, and at that time I brought out the point that the cone should always be carried completely up to the level of the internal os.



I think if you just amputate the cervix and the existing pathology in the pelvis persists, a cure may not be expected. We had about 75 or 80 per cent of retroversions, and 25 per cent of the cases which were operated upon had some adnexal pathology. If the cervix is amputated without correcting the existing pelvic pathology, that might explain a few of the cases which are unimproved or not cured at all.

DR. S. A. WOLFE.—Curettage, as a rule, was diagnostic in nature, for many patients presented menorrhagia and metrorrhagia in addition to cervical discharge. In the low infection cone group, cautery treatment would suffice for relief of symptoms but since rectocele and cystocele were to be corrected, excision of the cervix was simultaneously performed. In the entire series of 130 cases there were only 9 cases of excision without any other operative procedures. In the intermediate infection group cauterization would hold its own with surgery. In the completely infected cervix, the infected endocervix at the internal os would prove as inaccessible to the cautery point as to the surgeon's knife. The persistence of symptoms would result from retained infected mucosa. Cautery excision of the cervix was not practiced in this series.

Diagnostic curettage should be performed where malignancy is suspected even at the risk of poor end-results after excision.

Retroversion has little effect on ultimate cure. There were 59 cases in a series of 130 patients. Twenty were cured by vaginal fixation; the remainder by abdominal suspension. The end-result in cases of retroversion were coincidentally the same as in patients free from this condition. The operative correction has removed leucorrhea due to chronic passive congestion. Possibility of recurrence of discharge from an infected husband was not investigated even in the gonorrheal group. Recurrences, however, may occur from infected Skene's and Bartholin's ducts in the same patient.

DR. C. B. LULL, of Philadelphia (by invitation), read a paper entitled **An Analysis of One Thousand Obstetric Case Histories.** (For original article see page 75.)

#### DISCUSSION

DR. B. P. WATSON.—It is very desirable to hear some one say openly that he does not follow any one method, but that he chooses the method which he considers best for the particular case. I think a great deal of our medical practice today suffers from this habit of following the latest method indiscriminately. We have to teach conservatism, but we all in private practice do things which we would not teach to our students in the classroom or in the clinic. The great worth of Lull's paper is in bringing before us that we must not slavishly follow any set method, but must treat each individual patient as an individual and bring to bear on the treatment of that patient all the knowledge and all the clinical judgment that we possess. If the man has not it in him to do these things and to use good sound judgment, he never will be an obstetrician, a surgeon, or a physician. In other words, every man who really successfully practices medicine must have what I call clinical sense.

DR. H. C. WILLIAMSON.—I feel that it is rarely necessary to do version for an occipitoposterior, as the majority can be delivered by the single application of the forceps, rotation and delivery. Nor do I believe that it is dangerous to deliver an occipitoposterior as such. It is often a wise maneuver when the head is moulded well into the pelvis in the occipitoposterior position and especially if the pelvis is of the funnel type, which we commonly see in American women. I believe it is good obstetrics to do a generous mediolateral episiotomy and extract the baby in that position.

I cannot agree that the flap operation is more difficult than the classical one. In my hands it has given more satisfactory results.

DR. H. W. MAYES.—I would like to ask whether local anesthesia is used routinely in cesarean section and whether low mortality is due to its use.

DR. C. B. LULL.—I have to admit very frankly that I cannot do the low flap operation as well and as rapidly as I can the high operation. It is technically more difficult. When my mortality rate in cesarean section from the so-called classical or high operation goes above 2 per cent then I shall do all low cervical operations, but until then and until I have proved to myself that I am capable of doing the low operation as well as the high operation, I shall stick to what I am doing now.

In regard to version in posterior occiputs: I do not think there is any doubt that the labor caused by posterior rotation of the occiput is unquestionably prolonged, and there is no complication in obstetrics that I fear more. About four years ago, at the suggestion of Vaux, we ran a series of cases in which version was done early in posterior rotation of the occiput and our results were most satisfactory. I think that it is entirely a question of knowing when to do the version.

In reference to the delivery of a posterior occiput as a posterior occiput: it is very seldom that it is necessary to deliver a posterior occiput as such and even in spite of episiotomy, I have gotten some of the worst tears or what you might call traumatism of the pelvic floor, and usually of the rectum, in these cases if I have delivered them as posterior occiput.

In so far as the question of anesthesia is concerned in cesarean section, I do a very large proportion under local anesthesia. The ones that do not have local anesthesia I do under nitrous oxide until the child is delivered, and following that the woman has enough ether to relax her so that I never see the intestines.

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## OBSTETRICAL SOCIETY OF PHILADELPHIA

MEETING OF NOVEMBER 5, 1931

DRS. B. M. ANSPACH AND J. HOFFMAN presented a paper entitled **The Foundation of an Endocrine Clinic for the Study and Treatment of Amenorrhea, Uterine Bleeding and Sterility.** (For original article see page 3.)

### DISCUSSION

DR. P. BROOKE BLAND.—An example of the effects of x-rays is shown in a patient now under my care who had an amenorrhea of nine years' duration. She is thirty-three years old and typical of the ductless gland type, exemplified by excessive weight, coarse features, abnormal distribution of hair, and masculine configuration. Though married and exceedingly anxious to bear children, she had never conceived. At the beginning she was treated by a restricted dietary and along empiric organotherapeutic lines. There was no response. The husband was examined and found biologically normal.

The organotherapy was finally supplemented by stimulating doses of x-ray, applied alternately over the pelvis and sella turcica. After a relatively short time menstruation was reestablished, conception took place and the patient is now in her seventh month of an apparently straightforward normal pregnancy.

DR. W. E. CHAMBERLAIN (by invitation).—There is no such thing as a *stimulating* dose of x-rays, in the sense of a certain selected quantity of ray having a different or opposite action from a larger or smaller quantity. A few years ago, a

good many radiologists believed that while a large dose of x-rays or radium rays was inhibitory and destructive, a dose of from 2 to 30 per cent of that large dose might be "stimulating" to various cellular functions. This belief is without any foundation in fact.

In order to emphasize this point, let us consider the action of roentgen and radium rays upon organs and secretions and tissues that can be actually observed. The secretion of saliva, the activity of the secretory glands of the skin and mucosa, the secretion of gastric juice, all of these are decreased or depressed by large and moderately large doses of irradiation, and when we employ dosages too small to produce this depressant effect, the result is simply no effect at all. There is no sign of stimulation. The same may be said of the action of the rays upon tissue proliferation. Large doses inhibit, and doses too small to produce such inhibitory action, simply do not act at all, so far as we can discover.

There is a possible explanation for the reputation which the rays once had as stimulators. A patient with infiltration of both kidneys by Hodgkin's granuloma, developed almost complete anuria. The excretion of urine was promptly reinstated by a moderately intensive irradiation of the kidneys. This does not indicate any stimulative action of the rays. The favorable action upon the excretion of urine is readily accounted for by the regression in the abnormal tissue elements that were crowding and compressing the functioning kidney tissue and its blood supply.

If the menstrual function is governed by positive and negative factors, and we remove a part or all of a negative factor by the *depressant* or *inhibitory* action of x-rays, we may get the impression that x-rays are stimulating to the positive factor, while in reality the action, so far as the rays are concerned, is entirely inhibitory.

A word as to the general subject of x-ray exposures to the pituitary in cases of endocrine dysfunction. Without a doubt there are many proved cases of favorable results from such x-ray treatment of the pituitary. But a proper evaluation of such treatment will not be possible until we have collected statistics for large groups of cases, with several different technics in each group, and with a careful classification of each case. The tendency has been to try these treatments more or less at random, grouping together a number of different conditions which can hardly be placed in the same scientific category. Our own series of cases at Stanford University was fairly large, but was not well classified. Cases of amenorrhea, menorrhagia, frigidity, sterility, and ovarian hyperfunction, so called, were treated alike, and it was well nigh impossible to draw any accurate conclusions. I will have to limit my comment upon our results to the simple statement that our gynecologist believes that favorable results may follow irradiation of the pituitary in cases of amenorrhea and also in cases of menorrhagia. This is surprising, and if true, would seem to indicate that some sort of regulatory function of the pituitary may be reestablished or favorably modified by the irradiation.

In one regard, our statistics were quite convincing, and very surprising. A group of 100 cases, rather loosely classified as "ovarian dysfunction" were divided into subgroups "A" and "B," 50 in each. Two nozzles were built for the x-ray treatment tube shield, one of which was blocked off by a thick layer of lead, while the other contained the conventional copper filter to allow passage of the x-ray beam. The two nozzles were so built as to be identical in outward appearance and weight, and were put into service without anyone in the radiologic or gynecologic departments knowing which was which. With one nozzle labeled A and the other B we were thus able to divide our 100 cases into 50 treated and 50 untreated, without the possibility of psychic factors entering into our evaluation of the results.

The final evaluation was made about one and a half years after the treatments were begun, a year after the completion of the last treatment series. In only one particular were the resulting statistics convincing, namely in regard to fecundity-

For during the year and a half there were eight pregnancies among the cases in group A while there were none at all in group B. It so happened that group A received x-ray, while the blank nozzle was the one used in group B. Our statistician assures us that there is not one chance in a million of such a finding being due to pure chance. In other words, we have here very good statistical evidence to indicate that x-ray exposures to the pituitary region promote fecundity, and should therefore be tried out in cases of unexplained sterility. I should explain further that an investigation of all the cases indicated that opportunities for conception were very evenly divided between the two groups, almost all of the cases in both groups being married.

Our experiments were all carried out with a very definite dosage technic which was rigidly adhered to. Using the high voltage, copper-filtered ray, a square area 8 cm. by 8 cm. was exposed, over each side of the skull, centered very accurately upon the pituitary. At the first sitting we administered, at the skin, 125 r (measured in air, without scatterback). Calculating for the increment due to scattering, we have a dose of about 150 r at the skin, and calculating for absorption by the intervening tissues, the dose reaching the pituitary should have been about 100 r (50 r from each side). After this first exposure, we gave a series of five additional exposures, one week apart, administering 50 r (air measurement) to each side, at each sitting (about 40 r at the pituitary.)

The above dosage was chosen because slightly below the epilating intensity, 40 per cent weekly additional treatments being just sufficient to bring the accumulation in the skin up to the 150 r level at each treatment. (Skin recovery from x-ray treatments of this type amounts to approximately 40 per cent per week.) It should be explained that such a series of six exposures was designated "one full course." Usually only one such course was given. Occasionally a second course was given, but this was never done sooner than three months after the first course was completed.

Someone has asked me what the above dosage amounts to in terms of the oft-described "erythema dose." I can only say that the "roentgen" (r-unit) is a scientific and accurate measure of x-ray administration, while the designation "erythema dose" is almost devoid of meaning. I have measured the output of literally scores of treatment machines, and have found more than a hundred per cent of variation in the measured amounts of ray which constituted the doctor's conception of his "erythema dose." This is because erythemas may be observed or may not be observed, with dosages ranging all the way from 200 r up to 600 r, depending upon the patient, the size of area used by the observer, and the frequency and time of observations. It is to be hoped that we will soon hear no more talk of the "erythema dose." All dosages with roentgen rays should be measured and recorded in "r."

For those who have been recording dosages in other terms, we would suggest a calibration in "r." This is done by placing a calibrated ionization chamber in the x-ray beam while operating the machine at its usual setting.

DR. CHARLES MAZER.—Dysfunction literally implies alteration in the quality of an endocrine product. This, however, is not known to exist. The term therefore signifies a condition in which evidence of hypo- and hyper-activities of a given gland are simultaneously observed. This naturally pertains to those endocrine glands which produce more than one active principle. An excellent example of ovarian dysfunction is the prolonged and relative increase of female sex hormone by a persistent cystic follicle unantagonized by the lutein hormone, giving rise to endometrial hyperplasia and consequent abnormal uterine bleeding. Very rarely the persistent cystic follicle continues to produce enough hormone to maintain the uterine mucosa in a surcharged condition resulting in, what Zondek calls, hyperhormonal amenorrhea.

Doctors Anspach and Hoffman properly stress the importance of the anterior pituitary lobe secretions in initiating and maintaining the ovarian cycle upon which the uterine cycle depends. As to whether the gland produces two individual sex hormones, Prolan A and Prolan B, is still a matter of conjecture. My experimental experience leads me to believe in the existence of only one pituitary sex hormone. It is fallacious to assume that the injection of a small amount of Prolan B can produce luteinization of the infantile ovaries without previously stimulating the ovarian follicle to some degree of maturity. Moreover, the progestational phenomena in the endometrium of the test animal can occur only after previous priming with female sex hormone. Hence, the luteinizing hormone now at our disposal is apparently capable of producing both phases of the sexual cycle, follicular growth and luteinization.

This problem, though seemingly purely theoretical, is of great clinical importance. If the so-called luteinizing hormone has no effect on follicular growth, it can then be used only in cases of pseudomenstruation where the follicle matures but does not rupture, but cannot be used with any measure of success in cases where follicular growth is deficient.

DR. JOHN A. McGLINN.—Laboratory results in endocrinology are promising and yet, when we apply the newer products to the human being, the results are disappointing, clinically. This is especially noted when we attempt to control non-neoplastic bleeding or to regulate or substitute ovarian function.

I have tried out the Prolans of Novak in a number of cases and except in one case where the bleeding would stop for a day or two after the injection and then return, my results were entirely negative.

DRS. L. C. SCHEFFEY AND B. L. CRAWFORD described an **Adenocarcinoma of the Cervix in a Twenty-Two Months' Old Child**. (For original article see page 118.)

DRS. SCHEFFEY, MORGAN, AND STIMSON presented an **Analysis of a Series of 82 Cases of Ectopic Pregnancy**. (For original article see page 103.)

#### DISCUSSION

DR. EDWARD A. SCHUMANN.—A word as to the diagnosis. I believe that of all conditions in gynecology our method of procedure tells us more in this one than in any other. I believe the blood count to be of practically no value; sedimentation time is almost synchronous with acute inflammatory disease, and I was surprised to find the number of cases in which the suggestive finding of a pelvic mass was diagnosed. I have found in case after case no evidence of inflammation of the culdesac.

Autotransfusion takes too much time. This method may permit small clots of blood to enter the blood stream and is a definite menace to the patient in many instances.

DR. CHARLES A. BEHNEY.—Regarding the diagnosis, I would like to mention some observations in 167 cases studied at the University Hospital a few years ago. Masses were reported to have been present in 85 per cent of these cases. Softening of the cervix was described in 49 per cent, and the fundus was enlarged in 57 per cent.

Our prediagnostic errors, amounting to 38 per cent, were greater than in the series reported tonight. Fifty per cent of our erroneous diagnoses were pelvic inflammatory disease. Most of these diagnostic errors were in ectopic pregnancies

which had ruptured some time previously, and the secondary effects of the rupture overshadowed the symptoms of extrauterine pregnancy.

The postoperative complications included two cases of intestinal obstruction with one death; there was one abscess of the lesser peritoneal cavity followed by death from peritonitis and one patient developed typhoid fever three days after operation and died on the fourteenth postoperative day. There was one case of pericarditis; and one patient developed an abscess of the anterior abdominal wall. None of these patients died of the acute hemorrhage, and very few of the diagnostic errors occurred in patients who were actually acutely ill from the effect of hemorrhage.

The greatest difficulty in diagnosis, I think, is in obscure cases with some other complicating pelvic disease, or where abortion or rupture take place without causing alarming symptoms weeks or months before the patient comes under observation.

We considered the most reliable signs to be recurring pain, consistently in either iliac region, with a tender pelvic mass, irregular spotting, absence of temperature, practically normal pulse, no change in leucocytosis and a moderately rapid sedimentation time. After rupture we found that fainting was reported in about 50 per cent of our cases. Local pain, a progressive increase in the pulse rate, the leucocyte count, and the temperature, were considered the most reliable signs and symptoms. After the patient recovers from the shock of the hemorrhage she may have an increase in temperature. The diagnosis is usually easy when prompt operation is needed. When in doubt, time can be taken, without danger for careful study.

DRS. J. C. YASKIN AND I. ANDRUSSIER reported a case of **Syringomyelia Complicating Pregnancy and Labor**. (For original article see page 96.)

#### DISCUSSION

DR. PHILIP WILLIAMS.—I wish to report a case of syringomyelia occurring in a gynecological patient some years ago, in her early twenties, who complained of pain in the loin on the right side, urinary frequency, urgency, and cloudy urine, and it was found that she had a peculiar type of retention. After catheterization she would void from 16 to 20 ounces within a half hour. This happened a number of times. She was cystoscoped and the bladder findings were negative. The urine showed *B. coli* which, however, rapidly cleared up. Both her small toes had been amputated in 1917 when she was eight years old. This amputation followed a fall from a horse, the toes having become so contracted that she could not wear shoes, and to relieve this condition both the small toes had been amputated. She was admitted to hospital complaining of inability to bend her left knee or to flex the left ankle. A day or so later she was unable to move the right leg. There was loss of touch, pain, and temperature sensation up the left leg above the knee. On the right leg there was loss of tactile and pain sensation.

Three days later she was able to get out of bed, three days after that motion of the legs had improved, and a week later she was discharged with a diagnosis of paraplegia of the left leg.

The fact that she had loss of sensation of heat and cold made me feel she had some lesion of the cord.

Obstetric syringomyelia is referred to in Halban and Seitz' monumental work in only one instance, where it is said that hemorrhage of the spinal cord during the extraction of the fetus by the breech, or following version, may possibly be the occasion of some cavity formation in later life.

## BROOKLYN GYNECOLOGICAL SOCIETY

STATED MEETING, OCTOBER 2, 1931

**DR. ISIDORE DAICHMAN reported a case of Purpura Hemorrhagica Complicating Pregnancy.**

A. E., a primipara, aged twenty-seven years (last menses May 30, 1929, due March 6, 1930) was admitted to the Jewish Hospital of Brooklyn February 15, 1930 at 8 A.M. with a history of having had continuous cramps since 9 P.M. the night before. Membranes were intact; there was no bleeding or staining, and no history of toxic symptoms. Blood pressure at the time of admission was 115/80, pulse 84, red blood cells 3,900,000, hemoglobin 60 per cent. Urine was not examined on admission.

This patient had been to the prenatal clinic three times before her admission to the hospital. Condition normal.

At the time of admission to the hospital, abdominal examination revealed a fairly tonic uterus, tender to the touch. Fundus measured 29 cm. and no fetal heart was heard. Rectal examination showed the cervix to be well effaced, a little over one finger dilated, and a vertex well in the brim. A diagnosis of ablatio placenta with death of the fetus was made, notwithstanding the normal blood pressure, good pulse, and no evidence of bleeding.

She continued to have constant abdominal cramps and the pulse gradually rose to 100, but the patient looked well clinically and there was no external bleeding. About 12:30 P.M. it was accidentally discovered that the patient had an ecchymotic area over each anterior forearm where intracutaneous injections of some special test material had been made about two hours before. The blood pressure at this time was 130/84 and the urine showed a heavy cloud of albumin, with many hyaline and granular casts. The ecchymotic area suggested a blood dyscrasia and an immediate blood study was made by the Pathological Laboratory. The bleeding time was over two and one-half minutes, coagulation time four minutes, hemoglobin (Dare) 40 per cent, red blood cells 2,640,000, platelets 165,000, polymorphonuclears 91 per cent, lymphocytes 9 per cent, clot retraction, none after twenty-four hours.

At 1 P.M. patient received  $\frac{1}{2}$  grain of morphine.

Between 1 and 6 P.M., the pulse continued to rise until it reached 140, blood pressure varied from 130/84 to 140/84. There was still no evidence of any external bleeding. The lips were a bluish gray, while the face had a peculiar grayish color. At this time there was some bleeding from the gums. The uterus was still fairly tonic and the cervix was only one finger dilated. The pulse was of rather poor quality. A urea nitrogen done at this time was 16.4. Both the Medical Service and the pathologist saw the patient and concurred in the diagnosis of acute glomerular nephritis with a toxic purpura. Careful questioning of the patient and her relatives revealed a completely negative past and family history.

At 6 P.M. labor was induced by rupturing the membranes and inserting a No. 5 Voorhees bag into the cervix without anesthesia. The bag was expelled at 1:30 A.M. The head was perforated and the baby delivered at 2 A.M. The placenta was seen at the vulva immediately after the infant, and it was followed by about 300 c.c. of old blood and several large clots. Following delivery, blood pressure was 88/50; pulse was rapid and of fair quality. As the uterus remained flabby and atonic, it was packed at once with gauze soaked in mercurochrome. There was a first degree laceration of the perineum which was not repaired. The placenta showed a large area of infarction and thinning out, covering over half the maternal surface, and several blood clots were adherent to the thinned out area.

A transfusion of 350 c.c. of whole blood was given about one hour following delivery and the patient picked up nicely. At this time she had numerous ecchymoses

over the upper and lower extremities. The pulse gradually became fuller and slower and her general condition seemed to be improved.

Before delivery, hemoglobin (Dare) was 40 per cent, and red blood cells 2,200,000. After the transfusion, hemoglobin (Dare) was 50 per cent and red blood cells 2,180,000.

The next morning the blood pressure was 102/64, pulse 90-100 and of good quality. Urine showed a heavy cloud of albumin and many casts. The temperature on this day varied from 99° to 100° F., while the pulse fluctuated from 90 to 110. The patient looked very much improved. It is of interest that this patient began to improve immediately after transfusion and continued to do so day by day.

A second blood study done two days after delivery showed: hemoglobin (Dare) 34 per cent, red blood cells 2,384,000, bleeding time seven and one-half minutes, coagulation time two and one-half minutes, platelets 128,000, white blood cells 7,750, with a normal differential, and clot retraction time normal.

A blood chemistry showed normal figures, while the Kahn and Wassermann tests were both negative.

On the third day postpartum, a second transfusion of 300 c.c. of blood was given to combat the secondary anemia. On this day the urine showed only a faint trace of albumin and an occasional cast. The next day and every day after that the urine showed either no albumin or a very faint trace and no casts. The blood pressure varied from 108/60 to 118/68.

Examination of the eyegrounds four days after delivery showed the discs to be blurred in outline, especially on the right side. There was some connective tissue deposits around the blood vessels in the discs, but no hemorrhages or exudates were made out.

For the first six days postpartum, the temperature fluctuated between 99° and 101° and the pulse between 90 and 100. The only puerperal complication was a lochiometra which cleared up after a few days. After that the temperature and pulse were perfectly normal.

At no time was the spleen felt nor were any petechiae noted. The ecchymoses noticed before delivery cleared up within forty-eight hours.

The patient was out of bed on the eleventh day and went home at the end of the second week. A blood study done one day before discharge showed: hemoglobin (Dare) 42 per cent, red blood cells 3,600,000, bleeding time two minutes, coagulation time three minutes, platelets 400,000, white blood cells 13,000, with 68 per cent polymorphonuclears.

The patient was seen six weeks later, on March 29, 1930. Careful questioning and examinations showed that there had been no bleeding from any of the mucous membranes, and no petechiae or ecchymoses had appeared. The patient's color was good, the urine was completely negative, and the blood pressure 112/70. Spleen could not be made out. Pelvic examination revealed a healed first degree laceration, a slightly lacerated cervix, and a normally placed uterus well involuted. Blood chemistry was normal; Kahn and Wassermann tests were negative. Blood study showed: hemoglobin (Dare) 70 per cent, red blood cells 3,500,000, white blood cells 10,000 with a normal differential. Bleeding time normal. Coagulation time normal. Number of platelets normal. Clot retraction normal.

We were evidently dealing, in this case, with a latent toxemia of which the ablatio placenta and purpura were only symptoms. The purpura was not primary but toxic and as the toxemia cleared up, the purpura disappeared.

#### DISCUSSION

DR. HARRY KOSTER.—It seems to me that it is important to distinguish between the thromboecytopenic type and the nonthromboecytopenic type, because the treatment must be essentially different. In the true, essential thromboecytopenic type,



the only treatment of any value in a seriously ill patient, is splenectomy plus delivery. All the other types respond to emptying the uterus or treating the toxicity which is responsible for the hemorrhagic symptoms.

### DR. M. ROSENBERG reported a case of **Ectopic Gestation Following Modified Pomeroy Sterilization.**

Patient E. C., white, aged thirty-four years, was admitted to my service at The Jewish Hospital, on July 23, 1930, with a history of rheumatic endocarditis of several years' duration complicated by a five weeks' pregnancy, last menstrual period being June 13, 1930. Patient has been married sixteen years and has two children, the youngest six years old. The first child was delivered by instrument. The patient presented a mitral systolic murmur and tender joints throughout the body. The pelvic floor was relaxed, a slight cystocele, was present, the uterus anteroposed, somewhat enlarged and soft, the adnexa were negative. Because of the history of rheumatic endocarditis a therapeutic abortion and sterilization was decided upon.

On July 24, 1930, a dilatation and curettage was performed, followed by an anterior colporrhaphy through which was done a modified Pomeroy sterilization; that is, ligation and resection of a large loop of the cornual end of the tubes followed by electrocauterization of the severed ends of the tubes. Patient made an uneventful recovery and was discharged on August 5, 1930.

On December 5, 1930, patient was readmitted to Dr. Schwartz's service at The Jewish Hospital with the following history: Patient had two regular periods in August and September, following operation. The October period was delayed a few days so that patient resorted to medication, and began bleeding on November 10, 1930. The bleeding lasted about three days. However, on November 25, she began bleeding again, and on November 29 she experienced a severe sharp pain in the left lower quadrant, the pain being constant in character and associated with spotting and painful micturition.

Examination revealed marked abdominal tenderness with no rigidity in the left lower quadrant.

Vaginal examination revealed a firm parous pelvic floor with a well-healed firm anterior wall, a parous soft cervix that was tender on motion; the uterus slightly enlarged, was displaced anteriorly and to the right by a very tender small cystic mass in the left fornix.

Diagnosis of a left tubal pregnancy was made.

On December 6, 1930, a postvaginal section was performed, and free blood was found in the peritoneal cavity. This was followed by an immediate laparotomy. A median infraumbilical abdominal incision was made. The abdominal cavity was filled with a moderate amount of blood and blood clots. The omentum was found stretched and intimately adherent to both cornual ends of the uterus at the site of the previous resection of the tubes. The right tube was normal and separated from the uterus at its cornual end. The left tube which was the seat of an ectopic gestation was distended at its proximal end which was smooth and distinctly separated from the cornual end of the uterus. The two round ligaments were intact.

The omentum was freed from its adhesions and ligated. The left tube was freed from its adhesions, and a left salpingectomy was performed. The abdomen was closed in layers.

The tube was 7 cm. long, about two-thirds distended by blood clot 2 cm. in diameter, attached to the wall of the tube.

Microscopically, the tube was the seat of a chronic inflammatory process, contents consisting of blood clot and chorionic villi.

From the above case and those others reported in the literature it is evident that tubal ligation with resection is not an efficient measure to prevent conception.

Undoubtedly a fistula must have formed at either cornua of the uterus for conception to take place in this case.

DR. ELIOT BISHOP.—I would criticise Dr. Rosenberg's method of electro-cauterization of the stump, because a large cicatrix formed which sloughed away and following the slough fistula developed.

DR. MARTIN M. SHIR AND DR. I. DAICHMAN presented a paper entitled **The Use of Sodium Amytal in Labor.** (For original article, see page 115.)

#### DISCUSSION

DR. C. A. GORDON.—My experience has been rather small, about 20 cases in all, and nearly all of them characterized by the tremendous amount of restlessness described. It has seemed useless to us. Sometime ago we had almost the same experience with gas oxygen; the patients were markedly uncontrollable.

DR. I. DAICHMAN presented a paper entitled **Labor in the Elderly Primipara.** (For original article, see page 127.)

#### DISCUSSION

DR. S. B. SCHENCK.—I would like to ask the doctor how many cases of fibroids there were in this series. It is my impression that in elderly primiparae there are more fibroids than in younger women, possibly because they have not had repeated pregnancies until that time.

DR. DAICHMAN.—There were 11 cases of fibroids in this series; an incidence of 22.9 per cent. Of these, 7 patients were delivered by cesarean section and 4 by the vaginal route.

# Department of Reviews and Abstracts

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CONDUCTED BY HUGO EHRENFEST, M.D., ASSOCIATE EDITOR

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## Selected Abstracts

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### Physiology of Pregnancy

Abruzzese: Capillary Permeability in Pregnancy. *Riv. ital. ginec.* 9: No. 6, 1929.

The capillary permeability during pregnancy is increased; it reaches its maximum in the seventh month, decreases toward the end of pregnancy.

In puerperium there again is an increase in permeability which reaches its highest values on the third, fourth and fifth day. Then it decreases and reaches normal levels from the seventh to the eighth day.

The increase of the capillary permeability in the puerperium seems to be connected with the appearance of milk. In its origin one cannot well exclude hormonal factors, both mammarian and general, but the principal factors seem to rest with the neurovegetative system. The latter's functional significance may be defined as the establishment of a condition favorable to the migration of water and possibly other substances toward the mammae.

With the increase of capillary permeability in the puerperium there occurs disappearance of the hydremic plethora without increase of diuresis.

In the pluripara the capillary permeability is greater than in the primipara. Hydremia is increased in pregnancy, more in the primipara than in the pluripara, and most in toxicosis.

There exist relationships between hydremia and edema, but none can be demonstrated either between edema and capillary permeability or between capillary permeability and hydremia. Therefore, it seems difficult to attribute to this augmented capillary permeability any great importance in the pathogenesis of edema in pregnant women.

SYDNEY S. SCHOCHET.

JULIUS E. LACKNER.

Jakovleff, J., and Moshkoff, B.: Reticulo-Endothelial System in Pregnant Women. *J. akush. i zhensk. boliez.* 41: 6, 1930.

The authors were interested in determining the function of the reticulo-endothelial system in pregnant women. For this purpose they used 1 per cent Congo red solution for intravenous injection. Histocytes, moving cells of connective tissue, take the stain very easily. They are contained in the stroma of all organs, in the walls of vessels, in the skin and mucous membranes. To the interstitial connective tissue belongs the regulating rôle in metabolism. In this tissue are arrested the products of intermediary metabolism undergoing splitting and neutralization. Protein and lipid metabolism take place in a marked degree in the cells of connective tissue. The reticulo-endothelial system acts as buffer for parenchymatous organs. In those cases in which the ability for multiplication of the cells of connective tissue is de-

creased (hypoplasia of mesenchyme), or the fermentative ability is decreased, the rôle of the reticulo-endothelial system, as buffer, noticeably fails and danger for the parenchymatous organs increases. Therefore, as a preventive apparatus the reticulo-endothelial system, with advance of pregnancy, must become stronger. If the reticulo-endothelial system is not functioning completely, the organism becomes flooded with products of intermediary metabolism and this affects first the endothelium of the vessels, next the cells of the connective tissue and last the parenchymatous organs.

The study of the authors covers 71 cases, of which 58 were pregnant women and 5 had recently been delivered. As controls, six healthy, nonpregnant women and two women with gynecologic diseases were used.

The authors employed 12 c.c. of 1 per cent Congo red solution by the method of Reimann and Adler, using the colorimeter of Duboscq.

The Congo red index was: In healthy nonpregnant women, 34-53 per cent; nonpregnant women with gynecologic diseases, 74-86 per cent; pregnant, normal, first half of pregnancy 54-78 per cent; second half of pregnancy 60-75 per cent; pregnant with pathology, emesis 60-68 per cent; hyperemesis 71-90 per cent; slight nephropathia 62-67 per cent; marked nephropathia 79-80 per cent; grave cases of eclampsia up to 95 per cent; nephritis 60-80 per cent; heart lesions 60-81 per cent; mothers nursing their babies, 85 per cent; not nursing, 80 per cent.

ALEXANDER GABRIELIANZ.

**Haupt, W.:** Experiments in the Depth of Respiration During Pregnancy. *Ztschr. f. Geburtsh. u. Gynäk.* 96: 457, 1929.

Haupt determined the depth of respiration (Krogh technic) in 27 pregnant women who were all on a rigid low protein diet. Haupt corroborates the findings of Klawns and others, that the depth of respiration is increased during pregnancy. In the sitting posture, the depth is greater than when lying down.

LESTER E. FRANKENTHAL, JR.

**Gorony:** Blood Groups in Mother and Child and Their Relation to the Length of Pregnancy. *Ztschr. f. Geburtsh. u. Gynäk.* 97: 30, 1930.

The author typed the blood of 57 women and their offspring. In these cases the date of conception was definitely fixed. His results were as follows: (1) when the mother belonged to group A and the infant to group O, the duration of the pregnancy was decreased; (2) when the mother belonged to group O and the baby to group A, the length of pregnancy was increased.

LESTER E. FRANKENTHAL, JR.

**Nishizaki, S.:** Skin Pigmentation During Pregnancy. Its Significance for Parturient Women and Their Significance. *Japanese J. Obst. & Gynec.* 12: 371, 1929.

The author studied the skin pigmentation in 667 pregnant women. Five areas were compared and these were the face, the breasts, the chest, the abdominal wall, and the median line in the lower abdomen. The breasts showed the most pigmentation, then the median line, the face, the abdominal wall and finally the chest. This order persisted throughout pregnancy but the pigmentation in all the areas gradually increased in intensity as pregnancy advanced. Multiparas have a higher degree of pigmentation than primiparas.

J. P. GREENHILL.

# ITEM

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## AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY

**M**EMBERS of the Board and many of its Diplomates have been asked repeatedly about the purposes of the Board, the value of the certificate, its advantages to the Diplomates and other matters of general interest. For this reason it is planned to publish from time to time in the AMERICAN JOURNAL OF OBSTETRICS AND GYNECOLOGY, brief notes answering these and other questions which have arisen.

### THE BOARD

In 1930, after a period of organization covering approximately three years, the American Board of Obstetrics and Gynecology was established for the purpose of examining and issuing certificates to applicants who could demonstrate to the Board their proficiency in obstetrics and gynecology sufficient to warrant their being termed specialists in this branch.

The Board is officially sponsored by the American Association of Obstetricians, Gynecologists and Abdominal Surgeons; the American Gynecological Society; and the Section on Obstetrics, Gynecology, and Abdominal Surgery of the American Medical Association; and is composed of three Fellows elected from each of these three organizations. These nine representatives constitute the Board and serve as its examiners.

*Examinations are held annually (oftener when the number of applicants warrant) at the time and place of the meeting of the American Medical Association and are conducted by all nine members of the Board in order to assure impartiality in any and all decisions as to the certification of candidates. It has been suggested by many interested in the affairs of the Board that sectional examinations should be held, the work of examination being delegated to two or three individuals, already holding certificates and living in that section. The Board does not approve of such arrangement because it would put the onus of failures upon men who might be personally acquainted with candidates and therefore criticised for such action, and would also inevitably raise the question of lack of impartiality.*

The holding of examination-meetings of the Board in conjunction with the American Medical Association meetings enables the applicant to obtain reduced railroad fares and also to attend this important medical convention.

The names of the members of the Board as at present constituted are as follows: Dr. Walter T. Dannreuther of New York; Dr. Paul Titus of Pittsburgh and Dr. Grandison D. Royston of St. Louis representing the American Association of Obstetricians, Gynecologists, and Abdominal Surgeons; Dr. Jennings C. Litzenberg of Minneapolis, Dr. Joseph L. Baer of Chicago and Dr. E. A. Schumann of Philadelphia representing the American Gynecological Society; Dr. Fred L. Adair of Chicago, Dr. R. D. Mussey of Rochester, Minn., and Dr. E. D. Plass of Iowa City, Iowa, representing the Section on Obstetrics and Gynecology of the American Medical Association.

For further information address the Secretary, Dr. Paul Titus, 1015 Highland Building, Pittsburgh, Pennsylvania.

# American Journal of Obstetrics and Gynecology

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## Original Communications

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### THE CORRELATION BETWEEN THE DEVELOPMENT OF THE GROWTH AND THE SYMPTOMS OF CARCINOMAS OF THE UTERINE CERVIX\*

HENRY SCHMITZ, M.A., M.D., F.A.C.S., F.A.C.R., CHICAGO, ILL.

THE surgical and radiologic methods of treatment of carcinomas of the uterine cervix have been technically so perfected that further improvement can probably not be expected. The five-year absolute good end-results obtained with the present treatment vary from 20 to 25 per cent in the different clinics. The material unfortunately comprises a high percentage of advanced cases.

It is an undeniable fact that the percentage of good end-results varies inversely with the extent of the growth. The relative curability in the beginning, clearly localized cancers is about 75 to 90 per cent; in the doubtfully localized cancers about 35 to 50 per cent; in the cases involving the parametrium but retaining a fair degree of mobility about 10 to 25 per cent; and in the terminal, disseminated and fixed cancers zero. About 20 per cent of the total number belong to the first two groups and these show about 60 per cent of all the absolute cures, while about 80 per cent are seen in the last two groups, and these include only about 40 per cent of the good end-results. Improvement in the control of cancer obviously can only come from an earlier diagnosis and an institution of the indicated treatment without any delay. The avoidable delay in the treatment and the difficulties of the early diagnosis are responsible for the poor end-results of treatment. Indolence of the patient and negligence of the physician are only contributory causes. The control of cancer depends solely on early diagnosis and treatment.

Early diagnosis is an arduous task on account of the absence of

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\*Read at the Third Annual Meeting of the Central Association of Obstetricians and Gynecologists, October 29 and 30, 1931, at Chicago, Ill.

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NOTE: The Editor accepts no responsibility for the views and statements of authors as published in their "Original Communications."

symptoms in the beginning growth and the difficulties in the discovery of the beginning carcinoma nodule. All tumors must grow to some extent before giving symptoms. Could the cancer be diagnosed during the symptomless stage then control would be assured. If the physician would learn always to think of the possibility of the presence of a malignant growth and to study the macroscopic and microscopic characteristics, the extent of the growth development and the course of signs and symptoms, then early diagnoses would soon be made.

In an attempt to facilitate a study of early diagnosis an endeavor has been made to correlate the development of (1) the macroscopic appearance, (2) the microscopic findings, (3) the growth, and (4) the signs and symptoms. If one has observed a great number of cancers, then it appears that there is, as a rule, an orderly sequence in the developmental progress of a tumor from the beginning to the terminal stages in the four characteristics mentioned. The following facts also are generally conceded: (1) that cancer does not start in healthy tissue or organs; (2) that cancer begins in a spot or focus, the cells of which at first are not malignant; and (3) that chronic irritation causes this spot or works on this spot and produces the changes characteristic of malignancy.

#### THE MACROSCOPIC FINDINGS

The macroscopic picture of cancer varies depending on the type of growth, whether endophytic or exophytic. The sequence of changes in the endophytic type are nodule, ulceration, necrosis and finally sloughing with crater formation; while in the exophytic type the changes are nodule, papilloma, cauliflower growth with necrosis and finally sloughing with crater formation.

The cancer nodule is recognized with difficulty because benign nodules are more frequently seen than malignant nodules. It cannot be diagnosed by inspection or palpation. They do not cause symptoms. The Chrobak-Clark sign may be presumptive. If a nodule is touched with a dull pointed object and bright red blood appears and the arterial bleeding continues for some time, then one may presume that cancer is probably present. But a positive diagnosis rests on an immediate diagnostic excision within the surrounding healthy tissue of the nodule and an immediate frozen section diagnosis. Procrastination by observation must never be practiced.

The cancer ulcer and papilloma are, also, difficult to diagnose, because ulcers and papillomas are more frequently benign than malignant. The ulcer results from the peculiar tendency of the central carcinoma cells in the nodule to degenerate due to the poor blood supply. The papilloma tends to grow outward, but here also the central cells degenerate and early become friable. Such small ulcers and papillomas bleed when touched. This "contact bleeding" is the first symptom of cancerous tumors. A diagnostic excision should be made within the healthy tissues

followed by an immediate frozen section diagnosis to rule out or in malignancy.

Necrosis is manifested by friability of tissue. The growth now has the consistency of brain substance. The examining finger on withdrawal may bring out sufficient material for microscopic examination to corroborate the clinical diagnosis. The periphery of such tumors is indurated, nodular and clearly invades the adjacent tissues. Arrosion of blood vessels causes spontaneous hemorrhages, while the necrosis produces discharge.

Crater formation is an evidence of the extensive sloughing of the necrotic and friable tumor particles. The walls of such craters are irregular and indurated. The crater formation is indicative of an advanced stage and is almost invariably associated with wide dissemination into and fixation of tumor to the pelvic fasciae and bones. Pain is added to the symptoms of hemorrhages and discharge. It always signifies an invasion of the deeper pelvic structures or the adjacent organs by the cancer.

When cancer arises in situations not easily accessible to microbes it is a chronic disease and may not destroy the patient's life for many years. Cancer in protected sites often grows silently and unsuspected; but when it arises in situations easily accessible to putrefactive bacteria, for example in the alimentary or genital tracts, the primary lesion is readily colonized by bacteria. Such sequences soon manifest themselves and may speedily destroy the patient. The virulence of cancer, as a rule, depends not alone on the malignant character but also on its septicity. Putrefactive microbes are the common cause of failure in attempts to relieve cancerous patients by gross surgical and radiologic methods.

#### THE MICROSCOPIC CHARACTERISTICS

The histologic characteristics of a carcinoma in the sequence of their appearance are: (1) the atypia or anaplasia of the epithelial cells; (2) the invasion or breaking through of the basement membrane; (3) the destructive tendencies in displacing or assimilating normal tissues and cells; and (4) the formation of metastases either by continuity into the adjacent tissues and organs or by emboli either in the regional lymph nodes or distant sites. The microscopic diagnosis does not depend on the presence of all these factors. A diagnosis of cancer is justifiable without the evidence of metastation, it is still valid without the presence of destruction, and it is warranted in the absence of invasive tendencies. Early carcinoma is present when atypia or anaplasia alone are seen. The latter is characterized by a blurring of the cell mass, a down-growth of the epithelium with preservation of the basal layer, an abnormal behavior in staining qualities and an irregularity in the shape and size of the cells and the nuclei and a loss of polarity. Beneath the basal membrane and in contact with this new epithelium is an acute inflammatory exudate.



In the next step of development the round cells may break through the basal layer in places and thus come in actual contact with the most recently produced epithelial cells. The basal layer has failed in its protective function.

These atypic or anaplastic changes present the earliest evidence of the incidence of cancer in the human subject. This according to Bailey and Schiller is the moment of change from benign to malignant, the Cancer Phase. What proceeds thereafter does so in spite of any additional external factors which thenceforward are present, and is, in itself, progressive and inevitable.

Microscopic examinations of tissues removed by biopsy or by amputation of the cervix require serial sections if one expects to find evidences of cellular atypia or anaplasia. Otherwise it would be impossible to find very early carcinomas. It, also, precludes the treatment of suspiciously looking chronic cervicitides with the electric cautery, as the method might destroy such beginning cancerous foci. Therefore we are more and more inclined not to use the cautery method but to employ minor surgical procedures to obtain tissue for microscopic examination. Thereby one is placed in a position to rule out or in malignancy.

#### THE EXTENT OF THE TUMOR

The extent or growth development is determined by a general physical examination and a special pelvic examination. The latter comprises inspection by speculum and endoscopes, bimanual vaginoabdominal and rectoabdominal palpation, instrumental palpation with sound or curette, and eventually x-ray diagnostic procedures. Thereby the location and size of the growth, the condition of the parametria and adjacent organs such as vagina, bladder, and rectum, invasion of the regional lymph nodes and distant metastases are ascertained.

The following questions should be answered:

1. *Is the cancer clearly localized?* Such a beginning nodule should have a diameter of about 1 cm., should be clearly limited and freely movable within the cervix. The entire uterus possesses normal consistency, elasticity and mobility.

2. *Does doubt exist as to the absolute localization?* Such a tumor may have already spread to one-half of the cervical wall. It is surrounded by an area of inflammatory reaction enclosing dendritic processes of carcinoma tissue. The area is reddened, edematous and of doughlike consistency. Mobility of the uterus is impeded due to loss of elasticity of tissue, especially of the paracervical connective tissue.

3. *Are the parametria or regional lymph nodes involved and are the invaded structures mobile or fixed?*

4. *Have metastases or extensions occurred to bladder, vagina and rectum?*

5. *Has distant metastasis taken place?*

The answer to these five questions permits of a clinical grouping as follows: Group 1, the clearly localized growth; Group 2, the doubtfully localized growth; Group 3, the invasive growth; the invaded parametria or lymph nodes are movable; and Group 4, the disseminating and fixed growth including (a) the frozen pelvis; (b) invasion of bladder, vagina or rectum, and (c) distant metastases.

Inflammatory infiltration may complicate a uterine carcinoma. Nodular infiltration means carcinoma especially if the uterine tissue is continuous with the parametrial masses and the uterus is not displaced laterally, anteriorly, posteriorly, or superiorly. Fixation of the uterus occurs late in carcinoma and early in parametritis. It abates in the latter when resolution takes place. Coexisting tumors as ovarian cysts and uterine myomas may cause displacement of the uterus and impede its mobility though the carcinoma may be in the initial stage.

#### THE SYMPTOMATOLOGY

The sequence of symptoms in carcinoma depends on the extent of the growth. The clearly localized nodular growth is free from symptoms; the doubtfully localized, beginning ulcer and papilloma cause "contact bleeding"; the invasive, necrotizing carcinoma is accompanied by hemorrhage and discharge; and the crater-shaped, fixed carcinoma produces hemorrhage, discharge, and pain. It may be stated that hemorrhage is the earliest and most alarming symptom, discharge the most repulsive and constant symptom, and pain the most unfavorable symptom of cancer. A carcinoma causing pain is as a rule hopeless and incurable.

To the characteristic primary symptoms should be added the secondary or accessory symptoms resulting (1) from invasion of adjacent organs; (2) from compression of neighboring structures; (3) from toxemia due to the septicity of the cancer; and (4) from the cachexia occurring in all chronic and wasting diseases. Thus invasion of the bladder causes dysuria, pollakiuria, hematuria, and pyuria. Invasion of the rectum produces tenesmus, discharge, bleeding, and ribbon-like stools. Compression of the ureter terminates in hydronephrosis, eventually pyonephrosis with deep, constant, unbearable pain in the side affected. Septic infection is accompanied by pyrexia, putrid discharge, malaise, etc., while cachexia is characterized by an extensive katabolism, with rapid loss of weight and strength. Accessory symptoms are always suggestive of an advanced state of cancer and signify an absolutely poor prognosis.

#### THE CORRELATION OF THE HISTOLOGIC AND CLINICAL SIGNS

The various characteristics have been graded or grouped in numbers of four. If they are arranged accordingly, then Table I is obtained.

The conclusions may be drawn from Table I that the beginning nodule, the initial focus of carcinoma from which the disease progressively and inevitably develops, shows on microscopic examination a cellular atypia

TABLE I. CORRELATION OF THE HISTOLOGIC AND CLINICAL SIGNS

GROUP	MACROSCOPIC APPEARANCE	HISTOLOGIC DEVELOPMENT	THE GROUPING OF THE EXTENT OF THE GROWTH	THE SYMPTOMS
1.	Nodule	Cellular atypia	Clearly localized growth. Normal mobility of uterus.	None
2.	Ulcer or papilloma	Invasion of basement membrane	Doubtfully localized. Impeded mobility of uterus.	Contact Bleeding
3.	Large ulcer or cauliflower growth with necrosis	Destructive tendencies	Invasion of parametria or regional lymph nodes. The entire tumor mass is mobile.	Hemorrhage Discharge
4.	Crater	Metastasis, local or distant	1. Frozen pelvis with absolute fixation of tumor. 2. Local dissemination to vagina, bladder, or rectum. 3. Distant metastases.	Hemorrhage Discharge Pain

TABLE II. FIVE-YEAR END-RESULTS IN PRIMARY CARCINOMA OF THE CERVIX

CLINICAL GROUP	1	2	3	4	TOTAL
<i>a. All Cases up to 1927</i>					
Number	35	62	220	169	486
Total Number Five-Year Good End-Results	28	26	36	3	93
Percentage Five-Year Good End-Results	80.0	41.94	16.36	1.72	19.14
<i>b. Cases from 1924 to 1927</i>					
Number	12	14	61	69	156
Total Number Five-Year Good End-Results	10	6	18	3	35
Percentage Five-Year Good End-Results	83.33	42.85	26.23	4.35	22.43

of the epithelium, as yet devoid of invasion, destruction and metastation. The nodule is clearly limited and the uterus retains normal mobility. The growth has not thus far caused symptoms. These findings characterize the earliest stage of carcinoma. The diagnosis must be made by biopsy.

Perusing the following statistics it is seen that treatment in this stage shows a relative curability of 80 per cent. Treatment of cervical cancers during this stage, therefore, would place us in the control of cancer.

The observations that cancer does not start in healthy tissues or organs, and begins in a spot or focus the cells of which at first are not malignant; and that chronic irritation or inflammation causes this spot or works on this spot to produce the changes characteristic of malignancy, points to chronic cervicitis as a precursor of malignancy. The radical treatment of chronic cervicitis constitutes the best weapon against cancer, it is the prophylaxis of cancer.

According to Bailey, Schiller, Culbertson and others the first stage of carcinoma proceeds from a chronic cervicitis, which presents either

papillary erosions or follicular nodules. It results from an inflammatory subepithelial exudate which, not adequately fulminant to destroy the epithelial surface layer, causes the cells to proliferate forming erosions.

Bossi in 1913 discussed the true prophylaxis of uterine carcinomas and stated that chronic ulcers of the cervix and hyperplasia of the endometrium are precursors of carcinoma. He removed the diseased portion of the cervix by a low circular amputation and the hyperplastic endometrium by thorough curettage. Bossi did not observe a single cancer develop after many years of follow-up in about 7000 cases. Pemberton and Smith subjected all cervical tissue removed by operation to a systematic microscopic examination and found that 2.39 per cent of the cervix cancers were found by such examinations. During a period of fifty-two years, 5962 chronic cervicitides were treated, namely, 3814 with trachelorrhaphy, 740 cases with amputation, and 1406 with the electrocautery. Only 5 women developed cancer afterwards and in those cervixes treated with trachelorrhaphy. They found in 669 carcinomas only 12 cases which had had a cervical plastic operation. Hunner subjected 2895 cases of chronic cervicitis to either amputation or cauterization and after a follow-up for ten years not a single case of cancer developed.

These statistics prove the superiority of amputation and cauterization over trachelorrhaphy in the prevention of cancer. The latter reshapes the cervix but does not remove all abnormal cell changes which are located in the transition zone between the cervical canal mucous membrane and the vaginal mucosa.

Hinselmann in a discussion of the use of the colposcope in diagnosis of cervical lesions, records the following observations: (1) Normally the vaginal mucosa should end sharply and ringlike at the external os. It is seen in about 20 per cent of such examinations. Cancer is never seen in such cervixes. (2) An ectropic cylindrical cell mucosa does not predispose to carcinoma if the normal relations between vaginal and canal mucosae are maintained, though they are misshaped. Ectropion is usually due to a laceration without subsequent infection. They are observed in about 10 per cent of such examinations. (3) If a cervical erosion becomes chronic or heals, then a transition zone between the vaginal and canal mucous membranes forms, in which nodules or erosions may be seen. Such changes may become or are atypic and hence precursors of carcinoma. Such transition zones are present in about 70 per cent of such examinations.

Atypic changes in the transition zones are either composed of keratinized surface epithelial cells termed leucoplakias, or are desquamated areas devoid of pavement epithelium and may be recognized by Schiller's iodine test. Hinselmann saw about 2 per cent of leucoplakias or ulcerations which were considered atypical. Hence only two amputations would be indicated in 70 cases of chronic cervicitides. Whether these findings are correct the intensive studies with colposcopy will soon

demonstrate. At any rate unnecessary polypragmaty would thereby be obviated.

Schiller found in serial microscopic examinations of cervixes of 135 uteri removed for various pathology, but not cancer, four beginning carcinomas, that is, 2.96 per cent. During the same time 35 cervix and 5 body carcinomas were clinically diagnosed in 1549 consecutive gynecologic cases, that is 2.55 per cent. One may conjecture therefore that 2.96 per cent of carcinomas can probably not be diagnosed clinically and the incidence of carcinoma in gynecologic cases in the clinic would be 5.51 per cent. It may be followed that the careful investigation of the cervix will probably put us in the control of the cancers.

The question arises how may one find the symptomless, clearly localized and nodular stage of carcinoma of the cervix? (1) The profession should educate women to report for periodic health surveys after each labor and abortion, and yearly thereafter. If symptoms of leucorrhea, menorrhagia, or irregular bleeding should occur the patient should apply immediately for an examination. (2) The duty rests on the gynecologist, the teacher of gynecologic diagnosis, to provide facilities for instruction in diagnosis to the general practitioner in his clinic, so he may be taught to recognize a pathologic cervix. If the practitioner is well trained in diagnosis he may institute necessary procedures. If he cannot do so he should know that immediate expert consultation should be had. Delay for the purpose of observation is an error where carcinoma must be ruled out or in. If the beginning stage of cancer were not devoid of symptoms then the outlook for better end-results of treatment would be encouraging.

Time does not permit to discuss the discovery of early carcinoma of the cervical canal mucosa and the corpus. Sounding and diagnostic curettage are indispensable in these locations.

I am confident that the attack of the cancer problem made according to the views expressed would assure the control of cancer. The iteration of these truths may be elementary and not necessary in a meeting of specialists. However, the detection of the early stage of cancer is a difficult problem and the gynecologist must bear a great share of this responsibility.

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# FIVE-YEAR END-RESULTS IN THE (TREATMENT OF (CANCER) OF THE (UTERINE CERVIX AT THE BARNES HOSPITAL\*

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IN THE Gynecological Service of Barnes Hospital from July 1, 1921, to April 1, 1926, 138 cases of carcinoma of the uterus were treated by H. S. Crossen and myself. Of this number, 121 were of the cervix (108 squamous cell carcinoma and 13 adenocarcinoma) and 17 were of the body of the uterus. This series of 121 cases of cervical carcinomas form the basis of this statistical study. Of the 121 cases, 15 could not be located in the follow up. These lost patients were counted as dead from cancer. The 17 cases of carcinoma of the uterine body will be discussed in a succeeding paper. There were a few patients admitted to the service and treated by other gynecologists. Also, a few patients practically moribund, were admitted to the service but not treated. These cases were not included in this series.

In the preparation of this study the hospital record of each case was very carefully reviewed by me and an abstract of the case was made on a work sheet. This sheet contained all the data of importance pertaining to the case and from these work sheets facts were tabulated. When the patient was discharged from the hospital, if she was a private patient, she was advised to report to her respective physician for further observation and treatment. If she was a house case, she was advised to return to the gynecologic out-patient department for further care.

In the out-patient department, we maintain a gynecologic cancer clinic, in which there is a diagrammatic chart, giving the patient's name and date to return to the clinic. The patients are given an appointment card with the date marked on it when they are to return. They are instructed to return to the clinic every six weeks for the first year after receiving the initial treatment; every three months the second and third years; and every six months the fourth and fifth years. After five years has elapsed since the first treatment they are instructed to return to the clinic once a year. On each return to the clinic we examine the patients very carefully to determine whether or not more treatment is indicated. The treatment usually given after leaving the hospital consists of deep x-ray therapy to the pelvis and lower abdomen. The x-ray machine used is one of 200,000 volts. Rarely is radium repeated, though in a few cases, we feel radium repeated is more effectual than the deep x-ray therapy.

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The clinic cases are under the direction of the social service workers who see that they return at the appointed time. The follow-up in some instances has been difficult. Some patients move and leave no forwarding address and the social worker makes innumerable visits trying to locate them. Letters are sent to the patients and their physicians and neighbors and to postmasters and Red Cross workers in various towns and finally the bureau of vital statistics of the state in which they resided is consulted to see if they are listed as dead.

In this series of 121 cases, only 15 were lost in the follow-up, which is considered a fair record. Miss Ekka Gordon, social service worker, of the gynecologic service deserves much credit for her aid in locating the cases and when found living, getting them back to the clinic for examination. All of the living patients in this series have recently been examined by one of us and the accuracy of the pelvic findings vouched for. We believe that a follow-up that is conducted by the gynecologist himself is of far greater accuracy and therefore of more value in drawing conclusions, than is the follow-up by letter from the department to the patient or family physician.

We have found that the fact that the patient realizes she will be seen and examined by the person who operated upon her and who therefore, from her viewpoint, has a personal interest in her case will insure a high percentage of returns. In order to get the best cooperation of the patient, in most instances the patient is told she has cancer and the seriousness of the malady is explained to her. Of course, there are a few patients whose mental state is such it is best not to tell them, but rather explain the condition to some relative so they will see that she returns at the appointed time. We have realized for some time, that the greatest success is achieved by absolute cooperation from the patient. If they know they have cancer, regardless of the fact they have no suspicious symptoms after they have received treatment, they will return regularly for pelvic examination.

In figuring percentages of results, we consider that more accurate deductions can be made with greater simplicity if the patients are classified as living after five years. We think also, that percentages should be based on cases treated and consider as dead all those patients of whom we have lost track.

In studying this series of cases, there is a microscopic report of every case. The pathologic grouping by cell types was carried out by R. J. Crossen, who reviewed all slides.

Most gynecologists are now agreed that once a definite diagnosis of uterine cervical cancer has been made, the case is one for radiation or surgery. The patient should first be examined, not only to determine the extent of the local disease, but to ascertain the general condition of the patient. It is especially necessary to ascertain if any metastatic malignancy is present which will have a great influence on the treatment. Be-

Number of cases	108																							
Lost	12																							
Age	20-29.		30-39.		40-49.		50-59.		60-69.		70-79.													
	6		23		26		26		8		7													
Color	77—white				19—colored																			
Para	11—nullipara				10—primipara				75—multipara															
History cancer in family					8—yes		88—none																	
Duration bleeding before treatment							None		1-6 mo.		6-12 mo.		1-2 yr.											
							1		55		27		13											
Duration pain before treatment							None		1-6 mo.		6-12 mo.		1-2 yr.											
							18		58		18		2											
Type of cell	Sq. I.		Sq. II.		Sq. III.		indeterm.		adenocarcinoma															
	19		39		8		19		11															
Wassermann	11—positive				48—negative				37—none															
Mg. hr. radium	1600		1800		2000		2400		3000		3600		4000		4500		5000							
	2		3		9		4		33		5		19		4		17							
Number x-ray treatments.	Series				1		2		3		4		5		6		7		8		9		none	
					30		17		22		9		5		4		1		1		2		5	
Died from cancer											70													
Died within one year											28													
Died between one and three years											34													
Died after three to five years											8													
Died from other causes											2													
Alive and well after five years											24													
Cured from radium and x-ray therapy after five years											22.2%													



TABLE II. CLASS 4. CASES IN WHICH THERE WAS EXTENSIVE INVOLVEMENT OF THE UPPER VAGINAL VAULT INCLUDING THE BLADDER AND RECTUM. TREATMENT, X-RAY. NUMBER OF CASES 10

Number of cases	10
Lost	3
Age	20-29. 30-39. 40-49. 50-59. 60-69.
Color	1—white 1—colored
Para	1—nullipara 3—primipara 3—multipara
History cancer in family	7—none
Duration bleeding before treatment	1-6 mo. 6-12 mo. 1-2 yr.
Duration pain before treatment	3 3 1
Type of cell	Sq. I. Sq. II. Sq. III. indetermin. adenocarcinoma
Wassermann	1 2 3 4
Mg. hr. radium	6—negative 1—none
Number x-ray treatments	Series 1 2 4
	3 3 1
Died from cancer	7
Died within one year	6
Died between one and three years	1
Died after three to five years	0
Died from other causes	0
Alive and well after five years	0
Cured from deep x-ray therapy	0

TABLE III. SCHEDULE I. ANALYSIS OF CERVICAL CARCINOMA CASES CURED AFTER FIVE YEARS. NUMBER OF CASES 27

CASE NO.	NAME	COLOR	AGE	NUMBER PREG-NANCIES	DURATION BLEED-ING BEFORE TREAT-MENT	DURATION PAIN BEFORE TREAT-MENT
1	Mrs. M.	B	46	I	6-12 mo.	1- 6 mo.
2	Mrs. M.	W	39	None	6-12 mo.	6-12 mo.
3	Mrs. T.	W	63	VII	6-12 mo.	1- 6 mo.
4	Mrs. B.	W	43	II	1- 6 mo.	1- 6 mo.
5	Mrs. V.	W	43	VI	6-12 mo.	None
6	Mrs. A.	W	36	VII	1- 6 mo.	1- 6 mo.
7	Mrs. W.	W	55	V	6-12 mo.	None
8	Mrs. A.	W	38	II	None	None
9	Mrs. M.	B	47	III	1- 6 mo.	None
10	Mrs. A.	W	59	V	1- 6 mo.	None
11	Mrs. G.	W	45	III	1- 6 mo.	1- 6 mo.
12	Miss M.	W	50	None	1- 6 mo.	1- 6 mo.
13	Mrs. R.	W	43	II	6-12 mo.	None
14	Mrs. P.	W	28	III	1- 6 mo.	None
15	Mrs. K.	W	44	IX	1- 6 mo.	1- 6 mo.
16	Mrs. N.	W	45	I	6-12 mo.	1- 6 mo.
17	Mrs. H.	W	43	None	6-12 mo.	1- 6 mo.
18	Mrs. T.	W	53	V	6-12 mo.	1- 6 mo.
19	Mrs. G.	B	36	IV	6-12 mo.	None
20	Mrs. M.	W	54	X	1- 6 mo.	None
21	Mrs. L.	W	59	None	1- 6 mo.	1- 6 mo.
22	Mrs. P.	W	54	VI	6-12 mo.	1- 6 mo.
23	Mrs. H.	W	33	V	6-12 mo.	None
24	Mrs. K.	W	38	V	1- 6 mo.	1- 6 mo.
25	Mrs. G.	W	47	XII	6-12 mo.	1- 6 mo.
26	Mrs. G.	W	66	I	1- 6 mo.	1- 6 mo.
27	Mrs. T.	B	37	I	6-12 mo.	1- 6 mo.

radium were given and a few days later a radical abdominal hysterectomy was performed. Fourteen days after the operation a series of deep x-ray therapy was given. Three months later another series of deep x-ray therapy was given. At the present time the patient is living and well.

In the past five years we have not been so conservative in our classification and our operative mortality is much the same as many other investigators have reported.

In Class 3, there were 108 cases (Table I). By far the greatest number of cases treated came in this class. The treatment was radium and x-ray therapy and 24 patients lived five years and longer after receiving irradiation, 22.2 per cent cures.

In Class 4, there were 10 cases (Table II). They received deep x-ray therapy alone and not a single patient lived five years after treatment. The majority of the patients died within one year after treatment.

Tables III and IV, Schedules 1 and 2, show an analysis of the cervical

TABLE IV. SCHEDULE II. ANALYSIS OF CERVICAL CARCINOMA CASES CURED AFTER FIVE YEARS. NUMBER OF CASES 27

CASE NO.	NAME	CLASS	TYPE CELL	OPERATION AND DATE	MG. HR. RADIUM DATE GIVEN	SERIES X-RAY AFTER RADIUM	DATE LIVING
1	Mrs. M.	3	III	....	{ 2250 7-16-21 2250 9-16-21 }	4	4-10-1927
2	Mrs. M.	1	Indet	Rad. Abd. Hysterec. 7-14-21	None	None	2-10-1931
3	Mrs. T.	3	II	....	5000 3-10-22	2	2-10-1931
4	Mrs. B.	3	Indet	....	4000 3-27-22	2	2-10-1931
5	Mrs. V.	3	III	....	3000 4-24-22	2	2-10-1931
6	Mrs. A.	3	I	....	5000 5- 6-22	2	2-10-1931
7	Mrs. W.	3	I	....	5000 5- 6-22	None	2-10-1931
8	Mrs. A.	1	Ad-C	Rad. Abd. Hysterec. 6-22-22	None	None	2-10-1931
9	Mrs. M.	3	II	....	5000 7- 8-22	1	10-7-1927
10	Mrs. A.	3	Indet	....	5000 9-14-22	2	2-10-1931
11	Mrs. G.	3	II	....	5000 9-19-22	2	2-10-1931
12	Miss M.	3	II	....	2000 11-2-22	1	2-10-1931
13	Mrs. R.	3	II	....	3000 2-21-23	1	2-10-1931
14	Mrs. P.	2	II	Rad. Abd. Hysterec. 6-8-23	{ 1800 5- 5-23 2000 6- 3-23 }	2	2-10-1931
15	Mrs. K.	3	Indet	....	3800 6-11-23	3	2-10-1931
16	Mrs. N.	3	Indet	....	3000 8-23-23	1	1- 1-1929
17	Mrs. H.	3	Ad-C	....	3000 7- 8-24	4	2-10-1931
18	Mrs. T.	3	II	....	3000 8-11-24	3	2-10-1931
19	Mrs. G.	3	II	....	2000 10-2-24	3	6- 4-1930
20	Mrs. M.	3	III	....	3000 11-19-24	None	2-10-1931
21	Mrs. L.	3	I	....	1600 2- 4-25	4	2-10-1931
22	Mrs. P.	3	Indet	....	3000 9- 1-25	6	2-10-1931
23	Mrs. H.	3	I	....	4000 9- 8-25	1	2-10-1931
24	Mrs. K.	3	III	....	4000 10-21-25	1	2-10-1931
25	Mrs. G.	3	III	....	3600 11-27-25	4	2-10-1931
26	Mrs. G.	3	II	....	4000 1-31-26	2	2-10-1931
27	Mrs. T.	3	I	....	2000 3-26-25	4	3- 1-1931

carcinoma cases cured after five years. Total number of cases 27, cured per cent 22.3.

4 cases had never been pregnant.

23 cases had one or more pregnancies.

1 case had never been married.

1 case gave no history of bleeding before treatment.

12 cases gave history of bleeding one to six months before treatment.

14 cases gave history of bleeding six to twelve months before treatment.

10 cases gave no history of pain before treatment.

16 cases gave history of pain one to six months before treatment.

1 case gave no history of pain six to twelve months before treatment.

Two cases were adenocarcinoma and 25 were squamous cell in type. Of the 25 squamous cell carcinomas, 6 were in Group I cell type, 8 were in Group II, 5 were in Group III and 6 were indeterminate because of the marked necrosis of the specimens received in the laboratory.

Concerning the dose of radium. Two patients received 1600 mg. hr. and 1 patient is living. Nine patients received 2000 mg. hr. and 3 patients are living. Thirty-three received 3000 mg. hr. and 7 patients are living. Five patients received 3600 mg. hr. and 2 patients are living. Nineteen patients received 4000 mg. hr. and 4 patients are living. Seventeen patients received 5000 mg. hr. and 7 patients are living.

#### TECHNIC

The technic of application that we employ is as follows: The radium bromide salt is used. It is sealed in a glass capsule, this capsule is then placed in a silver capsule 1 mm. thick; the silver capsule is then placed in a brass capsule 1 mm. thick which is then placed in rubber tubing. In this form it is inserted into the uterine and cervical canals. If there is any chance of the radium getting out of position after its application, it is well to suture the cervix to hold it firmly in place. The dosage of 100 mg. is used (25 mg. in uterine cavity, 75 mg. in cervical canal) for twenty to fifty hours depending upon the amount of involvement of the cancer and the amount of tissue present for screening. Gauze is used to pack the bladder and rectum well away from the radium. In many cases a small rubber tube drain is inserted into the uterine cavity along side the radium to take care of any pyometra that may be present. A retention catheter is placed in the bladder in all cases. The silver, brass and rubber tubing screening of the radium is to filter out the harmful rays, and distance screening with vaginal gauze is for the protection of the bladder and rectum. With this technic, bladder and rectal fistulas are rarely seen.

#### SIGNIFICANCE OF THE RESULTS

There is a vast difference of opinion as to the indication for radium or operation. Many investigators feel radium should be used in all cases, others adhere to the classification similar to the one we have outlined. We feel each case should be classified before deciding on the treatment. We know that cancer is radium sensitive and radium resistant, the latter very rare, but does actually occur. So when early carcinoma is found we feel radical hysterectomy should be performed, unless the patient is a bad operative risk. Out of 121 cases only two cases were placed in Class 1

and 1 case in Class 2. The three patients were operated upon and today are living and well. In Class 3 we placed 108 cases. They received radium and x-ray therapy. The dosage of radium varying from 1600 mg. hr. to 5000 mg. hr. of this class, 24 (22.2 per cent) are living after five years. In Class 4 we placed 10 cases and they received deep x-ray therapy alone. None are living after five years.

In studying the statistics of large series of cases reported from several clinics both in America and Europe, one is struck by the fact that clinics where operation is the choice of treatment, show 20 to 30 per cent five-year cures. Also, clinics where irradiation is used entirely show similar percentage of cures. Radical hysterectomy, vaginal or abdominal, has been employed much longer than radium which has been used extensively the past fifteen years, and the fact that a comparison of the percentage of the cures is practically the same, makes us realize that with radium we have not made the progress in the treatment of uterine cancer we had hoped for. Apparently if we are going to reach that much heralded 50 per cent or more of cures by either operation or irradiation we must recognize cancer much earlier than we have in the past.

It seems obvious that the work of educating patients to seek a diagnosis at the very onset of suspicious symptoms is of importance, for it is clearly evident that the greatest percentage of cures is seen in the early cases. Also it is important that the family physician be alert and always on the lookout for symptoms suggestive of cancer and wherever possible make a vaginal examination.

In our gynecologic clinic it is interesting to note the number of early cancers of the uterus discovered in the past few years. All of the men working in the clinic are "cancer minded" and I am sure our next five year report will show more gratifying results than the present one.

#### SUMMARY AND CONCLUSIONS

1. Twenty-seven out of 121 patients lived five years or more after treatment, 22.3 per cent five-year cures.
2. The first symptom in the great majority of cases was vaginal bleeding.
3. The majority of the cases had bleeding or pain for six months before applying for treatment.
4. The greatest percentage of cures from radium was in older people, the younger the person the greater the mortality.
5. The greatest number of patients applying for treatment were in clinical Class 3. Twenty-four patients lived five years or more after treatment, 22.2 per cent cures.
6. Radium was effective in relieving hemorrhage and discharge in most of the cases.

## THE MODIFIED ASCHHEIM-ZONDEK TEST\*

P. F. SCHNEIDER, M.D., EVANSTON, ILL.

THE principles involved in the Aschheim-Zondek test for pregnancy have been presented so frequently and adequately that reiteration is unnecessary. The original method has received recognition as a diagnostic procedure of unusual accuracy, but, due to its technical difficulties, has unfortunately been denied the wide spread application which it merits. That the observations of Friedman,<sup>1, 2</sup> who was the first to call attention to the prompt ovulatory reaction in the rabbit following the injection of the urine of pregnancy, suggested a method of decreasing the technical difficulties of the test is evidenced by the numerous and diverse methods which have since been submitted.

The various phases of the substitution of rabbits for mice have been presented in considerable detail in the publications of Friedman and Lapham,<sup>3</sup> Reinhart and Scott,<sup>4</sup> Wilson and Corner,<sup>5</sup> Schneider,<sup>6, 7, 8</sup> and in the work of a large number of others whose results have as yet not been published. In spite of the fact that each of the above group of workers has obtained its results in a somewhat different manner, the technic in each instance has yielded results which have been comparable in accuracy with those obtained by the original method. In addition, the use of rabbits has decreased the time necessary for the completion of the test and considerably minimized the technical difficulties of the procedure.

A brief consideration of the essentials of the methods submitted will demonstrate more clearly their points of difference. Friedman and Lapham<sup>3</sup> advocate the use of adult female rabbits which have been isolated individually for a period of three weeks before being used. Five cubic centimeters of urine is injected three times daily for a period of two days time and autopsy is performed at the end of forty-eight hours. Friedman has demonstrated that frequent small injections of urine cause a greater stimulation to ovulation in the rabbit than a single large injection of equal amount.

Reinhart and Scott<sup>4</sup> use immature rabbits three months of age, weighing at least 3½ pounds each, and use a single injection of 5 c.c. of urine, followed by laparotomy at the end of twenty-four hours. If at this time a definite positive result is not obtained, the abdominal wound is closed, the rabbit reinjected, and operation repeated twenty-four hours later.

Wilson and Corner<sup>5</sup> advocate the use of adult female rabbits weighing 4 pounds or over, which have been kept in strict isolation for one month or more. The injection of 5 c.c. of urine is followed by laparotomy in not less than sixteen hours, at which time the positive diagnosis is dependent on the presence of freshly ruptured graafian follicles, laparotomy making possible repeated use of the same rabbit as early as two days thereafter.

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The technic suggested by me consists essentially of the use of immature rabbits four to four and a half months of age, with a single injection of 12 to 15 c.c. of urine, followed by autopsy forty-eight hours later.

Other proponents of the use of mature rabbits have suggested examination of the ovaries by laparotomy prior to the injection of the urine as an added safety measure in the elimination of false positives. This pro-

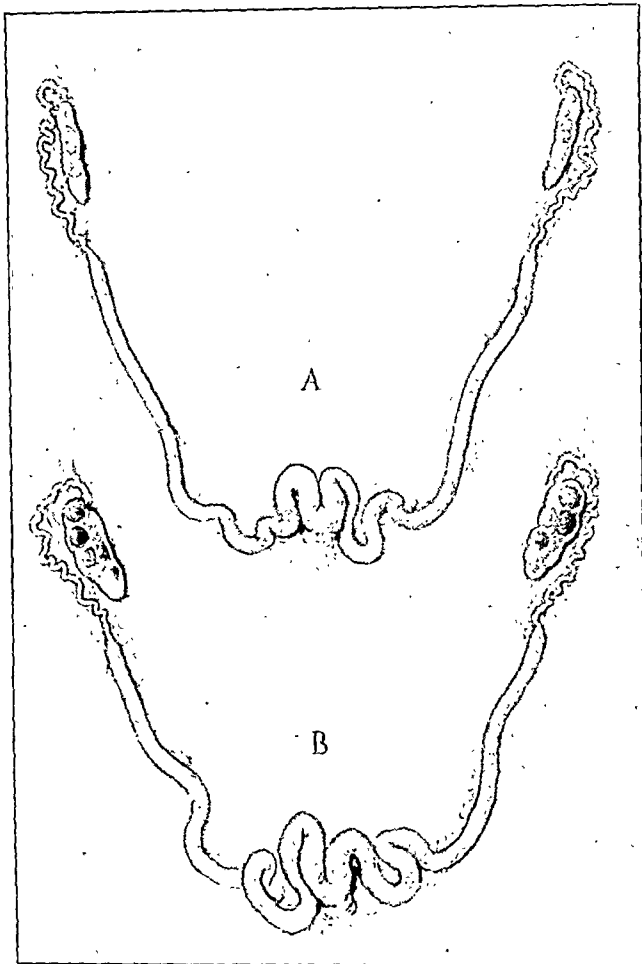


Fig. 1.—A, Corpora hemorrhagica and corpora lutea in the ovaries of an immature rabbit, resulting from the injection of the urine of pregnancy and demonstrating a positive result.

B, The normal ovaries of an immature rabbit, showing the cylindrical appearance of the ovary and the presence of visible follicles. This constitutes a negative result.

cedure has the advantage of necessitating individual isolation for a period of only eighteen hours.

#### DETAILS OF THE PRESENT SERIES

The present series of 500 cases in the application of the principles of the Aschheim-Zondek test for pregnancy by the use of rabbits, had its inception in the work of Friedman<sup>1, 2</sup> and was begun in January, 1930, the

first series of 100 cases being presented June 17, 1930.<sup>6</sup> Subsequently the test has been applied clinically in an additional 400 cases.

#### TECHNIC

The urine to be examined is obtained as a voided first morning specimen and, if possible, the patient is instructed to restrict fluids in an effort to obtain a sufficiently concentrated specimen. Routine filtration of each specimen prior to injection has completely eliminated the immediate mortality to the rabbit which has been encountered when cloudy nonfiltered specimens were injected.

The animals used for the test are obtained from a single reliable source of supply, are all of the same breed, and are known to be of an average age of four to four and a half months. The use of immature rabbits obviates the necessity of individual isolation, thus making it possible to maintain an adequate supply in rather limited space.

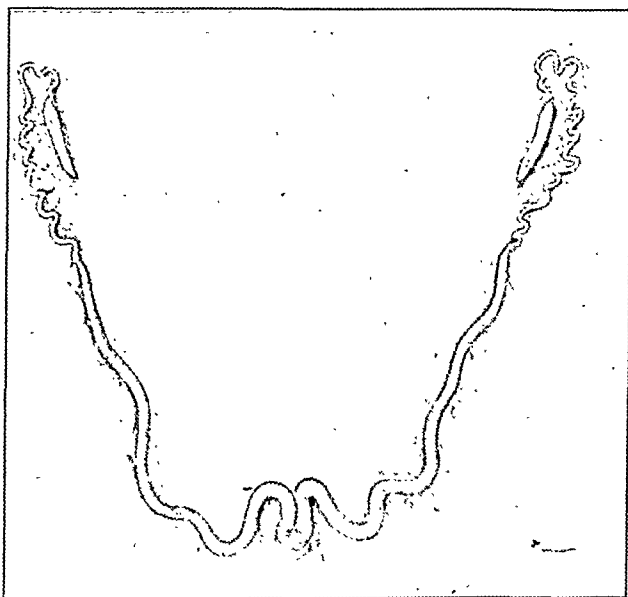


Fig. 2.—The ovaries of a rabbit not sufficiently mature to be satisfactory for the test and recognized by the opaque appearance, absence of visible follicles and flat or stellate conformation. Such an ovary at autopsy indicates an improper test animal.

Forty-eight hours following injection of 12 to 15 c.c. of the filtered urine into the marginal ear vein of the rabbit, autopsy is carried out and the ovaries inspected. The presence of definite corpora hemorrhagica or corpora lutea, or both, regardless of the number or whether present in only one or both ovaries, is accepted as a positive diagnosis of living decidua in contact with the maternal organism. (Fig. 1 A.) It is not necessary to determine whether rupture of the follicles has occurred when immature rabbits are used. In the absence of the above findings, further inspection of the ovaries should reveal a somewhat cylindrical ovary, showing the presence of many small unripe follicles visible in the substance of the ovary. (Fig. 1 B.) These findings constitute a negative result.

If, however, the ovary is small and flat or stellate, with a smooth opaque appearance, and there is an absence of visible follicles, it may be assumed that the ovaries of the particular rabbit used have not developed to sufficient maturity to respond to the stimulus of the hormone content of the urine. (Fig. 2.) Repetition of the test should be carried out before a diagnosis is rendered. The recognition of im-

mature ovaries in this manner has been found to be very essential, especially when it is impossible to obtain a reliable source of supply of rabbits, and the exact age of the test animals cannot be determined. It is also true that various breeds of rabbits mature later than others, while even a number of the same litter may show appreciable variations and abnormalities. Any one of the above factors may have been responsible for negative errors which have been obtained in some instances by other workers attempting the application of the test by using immature rabbits.

Autopsy, rather than laparotomy, has been selected as the method of choice in the present series of cases, due not only to the lack of facilities, but also to the fact that the lowered cost of immature rabbits does not seem to justify the expenditure of the time necessary to preserve the life of the rabbit.

## RESULTS

In an analysis of the 500 cases in which the above technic has been used, no conditions other than pregnancy or certain of its sequelae have yielded positive results. This may be of significance upon consideration of the fact that previous workers with the original Aschheim-Zondek test have in some instances reported positives resulting from conditions which are known to cause hypertrophy of the pituitary body, particularly the amenorrheas, both primary and secondary, and certain endocrinopathies. The above findings indicate that false positives may be considered as a negligible factor when immature rabbits are used.

False negatives have been obtained in only two conditions. The first of these occurred when rabbits were used which were not of the proper age or development. The second was due entirely to the limitations of the test.

In two cases a positive reaction has been obtained approximately three weeks following the intercourse responsible for the pregnancy. In three instances positive results have been obtained prior to a missed menstrual period, the preceding menses in each instance showing no variation from the normal.

On the other hand, negative reactions have been obtained from four to five days following a missed menstrual period in which repetition of the test four or five days later was followed by positive reaction. These findings demonstrate clearly the necessity for an accurate menstrual history in each case, so that a diagnosis will not be rendered until corroborated by a repetition of the test at a sufficiently late date.

The value and limitations of the test in abortion, missed abortion, hydatidiform mole, and chorionepithelioma have been presented in previous communications and by other workers, and further emphasize the necessity for careful consideration of clinical history and physical findings in the interpretation of results.

## DISCUSSION

The uniformly excellent results and comparative simplicity of technic provided by each of the four modifications suggested, emphasize the extent to which the substitution of rabbits has facilitated the Aschheim-



Zondek reaction and increased its availability as a diagnostic procedure, which does not necessitate a fully equipped laboratory and a high degree of technical skill.

This does not mean that the test is fool proof, and regardless of which method is used, absolute adherence to the details of the technic is a vital factor in its successful application.

Consideration of the various methods indicates that the selection of a method of choice will undoubtedly be influenced by the facilities which are available. If used in a well equipped laboratory, it is possible to keep large numbers of rabbits individually isolated and devote the time necessary to laparotomize the animals in each instance. Where these advantages are not available, it should be possible to establish a reliable source of supply of immature rabbits of a known age and permit autopsy to function as a time saving element.

#### CONCLUSIONS

1. The various methods utilizing the rabbit as a diagnostic procedure, when properly executed, yield uniformly accurate results.
2. When immature rabbits are used, the possibility of positive errors is rendered practically negligible.
3. The recognition of immature ovaries at autopsy, in addition to careful consideration of the physical findings and history, makes it possible to reduce the negative errors to a minimum.

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Itzkin, S.: The Tolerance of a Pregnant Uterus Duplex Toward Repeated Curettage of the Non-Gravid Half. Monatschr. f. Geburtsh. u. Gynäk. 84: 249, 1930.

The author searched the literature for cases of double uteri where a pregnancy remained undisturbed in one horn in spite of a curettage of the other nonpregnant horn. He found only four authentic cases and reports an additional one. In his case, the pregnancy was not interrupted though repeated curettements of the non-gravid half of the uterus had been done. To further emphasize the tolerance of double uteri the author discusses the cases where the decidua of the nonpregnant side was expelled long before the baby was born from the other half of the uterus and also those cases where pregnancies existed in both horns and the fetuses were expelled separately with a long interval of time between.

J. P. GREENHILL.

## OBSERVATIONS ON SECONDARY ANEMIA DURING PREGNANCY\*

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*(From The Mayo Foundation)*

ANEMIA is relatively common during pregnancy, especially in the later months. Lyons stated that among one-third of 200 patients examined in the third trimester, the concentration of hemoglobin was 70 per cent or less. Bland found that among 50 per cent of 200 patients, erythrocytes numbered 3,500,000 in each cubic millimeter of blood. A large majority of the cases of anemia of pregnancy are of a mild, secondary type.

Severe anemia complicating pregnancy is relatively uncommon. In reporting two cases of severe anemia of pregnancy, Evans stated that he did not see a case of severe anemia among women who represented 4,083 labors in the years 1926 and 1927. Pohl stated that geographic locality sometimes plays a part in severe cases of anemia, and he quoted Wolff, who reported 22 cases among 14,400 births in Zürich, only 8 cases among 90,000 births in Vienna in thirty years, and 27 cases in Parma in three years.

As Pepper pointed out, much of the literature on the subject of anemia of pregnancy antedates modern hematology, thus leading to much confusion between the so-called pernicious anemia of pregnancy and true primary pernicious anemia. Among recent writers, Brault, Devraigne and Laennec, and Audebert and Fabre used the term "pernicious anemia of pregnancy"; others, including Evans, Murdock, Rowland, Bland, Esch, Pohl and Alder have preferred the term "pernicious-like anemia of pregnancy." Pepper stated that in none of forty undoubted cases of pernicious anemia among women, at the University Hospital of the University of Pennsylvania, was there any relationship between pregnancy and the occurrence of the anemia.

Mention may be made, briefly, of other types of anemia which may rarely complicate pregnancy; hemolytic icterus, leucemia, purpura hemorrhagica, aplastic anemia, and hemophilia. Also, more or less severe grades of secondary anemia may be the result of loss of blood, frequent childbearing, and complicating conditions such as syphilis, pyelonephritis, toxemia, chronic nephritis, puerperal infection and tuberculosis. Husfeldt reported a severe case of anemia in pregnancy due to lead poisoning.

Alder postulated that preexisting chlorosis due to deficiency of bone marrow is responsible for severe grades of anemia and that the strain

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of pregnancy results in lowered capacity of the function of bone marrow. Others consider chlorosis merely a result of deficiency of hemoglobin. Hofbauer suggested that there is a syncytial hemolysin which if not counteracted by autolysin, results in destructive anemia. Larra-bee in his excellent classification of various etiologic hypotheses also included the hypothesis that isoagglutinins of the fetus, when incompatible, may cause toxemia or hemolysis in the mother.

Since many pregnant women have some degree of anemia, it may be assumed that a toxic factor, the result of pregnancy, or failure of physiologic adjustment, is the cause of the anemia. Kühnel reviewed the subject and studied the morphology of the blood of fifteen normal healthy pregnant women and concluded that there is a true anemia of pregnancy. Others have stated that the hemoglobin content of the blood is normal or slightly increased in the later months of pregnancy.

From the hematologic standpoint practically all anemia of pregnancy belongs to either one of the two general types of secondary anemia.

Type I anemia in which bone marrow is apparently deficient in activity, is most commonly seen. It is characterized by a moderate reduction in erythrocytes with approximately an equal decrease in hemoglobin. Morphologically, the erythrocytes usually show slight hypochromasia (practically normal), moderate anisocytosis, and varying degrees of polychromatophilia, depending on the degree of anemia present.

In early pregnancy there seems to be suppression in activity of bone marrow, as evidenced by the proportion of reticulated erythrocytes in the blood. In the later months of pregnancy the bone marrow apparently becomes hyperactive. The reticulated erythrocytes increase, yet fail to bring the blood count back to normal. This continued anemia in the later months of pregnancy, in spite of increasing numbers of reticulated erythrocytes, is probably due to some hemolytic agent. That a toxic agent is present is evidenced by the neutrophilic leucocytes which present varying degrees of toxicity, as shown by moderate shift to left, swelling of the nucleus, cloudiness of the chromatin and irregularity in distribution of the specific granulation and intensification of the staining reaction of the individual granules.

Type II anemia differs from Type I in one respect only; the hemoglobin is much more reduced in proportion to the reduction of erythrocytes, resulting in a marked hypochromasia, that is, the deficiency type of hemoglobin from the morphologic standpoint. The other features are approximately the same as in the Type I. Evidence indicates that Type II anemia is usually present prior to pregnancy and grows worse during pregnancy. It frequently persists following delivery and usually requires treatment.

A morphologic study was made of the blood of 82 pregnant women in whom the concentration of hemoglobin was below 70 per cent by the Dare method. Further hemoglobin readings and study of the blood cells

were made in most instances during and after pregnancy. Some of the patients were treated with extract of bone marrow and some with powdered fetal liver during the course of pregnancy. Later certain patients with anemia during pregnancy were treated with ferric citrate or ferric ammonium citrate.

The anemia of 58 of the 82 patients was classified as Type I, of 16 as Type II; 7 patients manifested changes characteristic of both types, and the anemia of one patient could not be classified.

Evidence of toxicity was found in 41 of the 58 cases of Type I, in only 11 of which was it more than of mild degree. It was noted in 10 of the 16 cases of Type II, in 6 of which it was well marked; and it was noted in 4 of the 7 cases of Types I and II.

The toxic factor or factors causing changes in blood cells was not determined. However, a search for possible contributing causes showed that 4 patients had pyelonephritis, 2 had had mild influenza; 2 had infected tonsil tags, 7 had some evidence of periapical dental infection; one patient had infected tonsils with chronic mitral endocarditis (compensated), and one had acute infectious arthritis and infected tonsils. Of 9 cases, the anemia in 4 was classified as Type I, and in 5 as of Type II; hematologic evidence of toxicity was marked. In all but 2 of these cases evidence of probable etiologic factors was demonstrated. Three of the patients had pyelonephritis, one of whom had also healed lesions of pulmonary tuberculosis; one patient had chronic mitral endocarditis and infected tonsils, one had had severe hyperemesis in the first trimester, one had had splenectomy for purpura hemorrhagica two years previously, and one had residual evidence of acute infectious arthritis and infected tonsils. Following tonsillectomy during the pregnancy of this patient the hemoglobin rose from 57 to 84 per cent in the course of ten weeks.

An extract of bone marrow obtained from a pharmaceutical firm was given in doses of 2 gr. three times a day to most of the patients with anemia of Type I. Subsequent use of extract of bone marrow indicated that much larger doses could have been used. Powdered fetal liver in teaspoonful doses in grape juice three times a day was given to some of the patients with anemia of Type II. In some instances even this small dose caused nausea and had to be discontinued.

In 24 of the cases of anemia of Type I and in 5 of those of Type II, estimations of hemoglobin were made to determine whether increase in the hemoglobin content of the blood was affected by the use of the drugs. In only 7 of the cases of Type I and in two of those of Type II was there a definite elevation of the hemoglobin. Later ferric citrate or ferric ammonium citrate in 20 to 30 grain doses three times a day was used in 20 cases of similar anemia, and 16 patients showed definite improvement. In a control group of 35 cases with secondary anemia of pregnancy in which treatment was not given aside from diet, spontaneous improvement occurred in 9. In these untreated cases the average concentration

of hemoglobin was 65 per cent in the first trimester, 57 per cent in the second, and 56 per cent in the third. In the cases treated with bone marrow or fetal liver the concentration of hemoglobin was 61 per cent in the first trimester, 57 per cent in the second, and 55 per cent in the third. In those treated with ferric citrate or ferric ammonium citrate the concentration of hemoglobin was 61 per cent in the first trimester, 63 per cent in the second, and 66 per cent in the third.

## COMMENT

This is a preliminary report of observations on secondary anemia during pregnancy. This is relatively common and there is a tendency for it to increase as pregnancy progresses.

Usually secondary anemia may be classified in two general types, the most common of which is Type I. In fact this type of secondary anemia seems to be true anemia of pregnancy, characterized by suppressed activity of bone marrow early in pregnancy and by evidence of hemolysis when the bone marrow becomes more active in the later months. There is a tendency for patients to recover spontaneously after delivery. It seems probable that severe cases of this type of secondary anemia make up a large part of the cases which have formerly been termed "pernicious" or "pernicious-like" anemia.

It seems probable that the Type II anemia is present prior to pregnancy, grows worse during pregnancy and persists after delivery. The use of organotherapy such as extracts of bone marrow and powdered fetal liver was not followed by appreciable improvement in this group of cases. However, this may have been due to insufficient dosage or inability of the patient to take the product. The use of ferric citrate or ferric ammonium citrate in large doses, 20 to 30 gr. three times a day, was followed by distinct elevation of hemoglobin in 75 per cent of a small group of cases.

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# A STUDY OF THE DEATHS FOLLOWING 6022 GYNECOLOGIC OPERATIONS\*

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IN THIS paper is presented a brief analysis of the deaths which occurred on the Gynecological Service of the Cook County Hospital from January 1, 1926 to January 1, 1931. Some difficulty was encountered in obtaining all the records, and there was still more hardship in attempting to find the actual cause of death in some of the cases. To do this, I utilized not only the internes' records but also the nurses' notes, the anesthetists' records, the reports of the pathologic tissue which was removed and the autopsy reports. In spite of this some of the combined records were incomplete and I had to surmise the cause of death in these cases. There were only 40 autopsies in this series of 213 deaths. However this incidence of 18.8 per cent for autopsies during the five-year period studied is not much below the frequency of postmortems at the Cook County Hospital for all the services. Thus during 1929 the total incidence of autopsies at this hospital was only 22.1 per cent, in 1928 it was 19.3 per cent, in 1927 it was 21.9 per cent, and in 1926 it was 21.8 per cent.

During the five-year period under consideration there were 6,022 operations of which 5,308 or 88.1 per cent were major and 714 or 11.9 per cent were minor in character. In this series there were 213 deaths, an incidence of 3.5 per cent. The distribution of the operations and the death rate according to each year is shown in Table I.

TABLE I

YEAR	NO. OF OPERATIONS	NO. OF DEATHS	MORTALITY
1926	1150 { 1027 major 123 minor	39	3.4 per cent
1927	1274 { 1167 major 107 minor	44	3.45 per cent
1928	1202 { 1034 major 168 minor	38	3.15 per cent
1929	1168 { 1023 major 145 minor	52	4.5 per cent
1930	1228 { 1057 major 171 minor	40	3.3 per cent
Total	6022	213	3.5 per cent

## TYPE OF PATIENTS

At the Cook County Hospital all the patients are charity patients. This means that a large proportion of them are admitted in very poor

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physical condition. Usually they have an advanced condition of the illness which forces them to go to the hospital and many of them are poor operative risks. In many cases, necessary operations are deferred until the patient's general condition can be built up by bed rest, proper food, care of the bowels, care of the teeth, and when necessary blood transfusions. Most of the patients operated upon on the gynecologic service were kept in the hospital at least four days before their operation was done. Women who had an elevation of temperature were usually kept in bed and operation postponed until the temperature was normal for at least five days. In some cases this rule was not observed, some women being operated upon in spite of a slight fever, but in other instances, operation was deferred for a much longer time than five days. Consultations with attending physicians in other departments were seldom had, except for gross abnormalities of nongynecologic conditions.

About half of all the patients on the gynecologic service are negroes, and many of them as well as a fair number of white women have a four-plus Wassermann reaction. A very large proportion of the negroes have more or less extensive pelvic inflammatory disease associated with other gynecologic conditions, and this has a distinct tendency to increase the risks of operation.

Some patients were operated upon by the gynecologists for conditions which were not gynecologic. Thus several of the patients with intestinal obstruction were brought to the operating room as emergency cases and operated upon by the gynecologists. Likewise patients with appendiceal abscesses, gall bladder conditions, and urologic afflictions were operated upon on the gynecologic service. All these cases and the fatalities are included in the present analysis.

The 6,022 operations reviewed were performed essentially by the six attending gynecologists. A moderate number were done by two alternates and a fair proportion were performed by the senior internes under the supervision of the attending physicians.

#### MORTALITY ACCORDING TO TYPE OF OPERATION PERFORMED

A list of the most frequent operations performed and the mortality associated with these operations is given in Table II.

In Table II is listed only the most important operation which each patient had. Frequently the operation given in the table was only one of two or more operations. Thus, most of the women who had a suspension of the uterus also had a plastic operation or a dilatation and curettage or an appendectomy, but only the suspension is listed in the table. Not infrequently the accessory operation and not the chief operation was the one which caused the death. Thus, it occasionally happened that the removal of an appendix caused the death of a patient who might otherwise have recovered.

The most frequently performed operation was abdominal supracervical hysterectomy. Most of these uteri were removed because of fibroids.

The adnexa were normal and were therefore left in place. The removal of the body of the uterus alone even if it is very large is usually a simple procedure and accounts for the low mortality of 0.8 per cent for the 747 operations.

TABLE II. MORTALITY FOR THE DIFFERENT OPERATIONS PERFORMED

TYPE OF OPERATION	NUMBER	DEATHS	MORTALITY PER CENT
Abdominal supracervical hysterectomy	747	6	0.8
Abdominal supracervical hysterectomy, bilateral salpingo-oophorectomy	661	59	8.9
Abdominal panhysterectomy, bilateral salpingo-oophorectomy	350	15	4.3
Abdominal defundation of uterus and salpingectomy	449	18	4.0
Abdominal panhysterectomy	201	11	5.5
Suspension of uterus	535	4	0.7
Salpingectomy	344	6	1.7
Salpingo-oophorectomy	281	7	2.5
Vaginal plastic operations	329	4	1.2
Vaginal panhysterectomy	158	3	1.9
Exploratory laparotomy	133	7	5.3
Appendectomy	123	3	2.4
Oophorectomy	115	4	3.5
Colpotomy	89	8	9.0
Trachelorrhaphy or amputation of cervix	76	2	2.6
Myomectomy (abdominal and vaginal)	53	3	5.7
Biopsy	31	12	38.7
Colostomy	14	11	78.6
Vulvectomy	13	2	15.4
Watkins-Wertheim interposition	21	0	0
Cholecystectomy	8	0	0
Vesicovaginal fistula	7	1	14.3
			186

On the other hand operations complicated by the presence of tubal and ovarian infections are attended by a high mortality. Thus, among the 661 operations where both the body of the uterus and the adnexa were removed, the death rate was 8.9 per cent. In the large proportion of these cases, the adnexa were inflamed, thickened, and adherent to nearby structures and organs. Frequently their removal was a dangerous procedure because of their adherence to the bowel or bladder. In many of the cases the uterus was amputated only because both tubes and ovaries were so badly diseased that they had to be removed, whereas in other cases, the indications for the hysterectomy was the presence of fibroids, fibrosis uteri, etc.

There were 350 operations in which the body of the uterus, the cervix, and the adnexa were removed and the mortality was 4.3 per cent. In most of these cases either the cervix was diseased, the adnexa were pathologic, cancer of the body of the uterus was present, or there were fibroids.

The large group of 449 defundations was performed almost exclusively in young women who had bilateral salpingitis. The purpose of this op-



eration was to remove the tubes and the fundus, so that all the diseased portions might be eliminated. One or both ovaries was left and also a sufficient portion of the body of the uterus, so that the woman might menstruate. In the group of 449 defundations, there was a death rate of 4 per cent.

Abdominal panhysterectomy was performed 201 times and the mortality was 5.5 per cent. This is a high death rate for a relatively simple operation. Most of these cases were fibroids associated with pathologic cervixes.

In the series of vaginal panhysterectomies, the mortality was 1.9 per cent. This was one-third the death rate for the group of uncomplicated abdominal panhysterectomies. The number of vaginal hysterectomies was not greater because a large proportion of the women, especially the negroes have pelvic inflammatory disease which makes vaginal operations difficult and dangerous to perform.

The 133 exploratory laparotomies had the high death rate of 5.3 per cent, but this was chiefly due to the fact that many of the patients had inoperable cancers or other conditions apart from the operation which caused their death.

The mortality for the 115 oophorectomies is high as is also the death rate for the 89 colpotomies, for the 53 myomectomies, and for some other operations. There were many fatalities among the biopsy cases because many of these patients had inoperable carcinomas. The pieces of tissue were removed not only from the cervix, but also from the vulva, the rectum, and from within the abdomen.

The death rate for the colostomy operations was necessarily high because nearly all these patients were brought to the operating room in critical condition as emergency cases due to intestinal obstruction. The vulvectomy operations were performed for cancer of the vulva or for kraurosis vulvae.

TABLE III. OPERATIONS PERFORMED ON REMAINDER WHO DIED

Resection of intestines	6
Plastic on tubes	3
Removal of Bartholin abscess	2
Cauterization of ovaries	2
Dilatation and curettement	2
Abdominal and vaginal drainage	1
Repair of bowel	1
Transplantation of ovary	1
Panhysterectomy and ligation of veins	1
Panhysterectomy and radium	1
Removal of papilloma of bladder	1
Repair of ventral hernia	1
Drainage of perinephritic abscess	1
Closure of vaginofecal fistula	1
Repair of rectovaginal fistula	1
Lymphangoplastic	1
Hemorrhoidectomy	1
	—
	27

A list of the operations performed on the 27 fatal cases not included in Table II is shown in Table III.

## ANALYSIS OF DIAGNOSES

The operative diagnosis of the 213 deaths is listed in Table IV. The largest number of deaths occurred following operations for fibroids of the uterus, pelvic inflammations, and malignancy.

TABLE IV. OPERATIVE DIAGNOSIS OF THE FATAL CASES

Fibroid uterus	69
Salpingitis and pelvic inflammation	65
Malignancy	31
Ovarian cyst	13
Intestinal obstruction	11
Cystocele and rectocele	8
Appendiceal abscess	3
Fistula	3
Prolapse of uterus	2
Pyometrium	2
Bartholin gland abscess	2
Ventral hernia	1
Hemorrhoids	1
Perinephritic abscess	1
Pregnancy	1
	<hr/> 213

The operations performed on the 69 fatal fibroid cases are given in Table V.

TABLE V. OPERATIONS FOR THE 69 FIBROID CASES

TYPE OF OPERATION	NUMBER
Abdominal supracervical hysterectomy, bilateral salpingo-oophorectomy	43
Abdominal panhysterectomy	10
Abdominal panhysterectomy, bilateral salpingo-oophorectomy	3
Abdominal supracervical hysterectomy, bilateral salpingectomy, unilateral oophorectomy	4
Myomectomy	3
Abdominal supracervical hysterectomy	4
Defundation, bilateral salpingectomy	2
	<hr/> 69

The causes of death in these 69 cases are shown in Table VI.

TABLE VI. CAUSE OF DEATH IN THE FIBROID CASES

CAUSE OF DEATH	NUMBER	PER CENT
Peritonitis	35	50.8
Embolism	9	13.0
Hemorrhage and shock	8	11.6
Myocardial failure	7	10.1
Pneumonia	5	7.2
Uremia	2	2.9
Pyelocystitis	1	1.4
Encephalitis or meningitis	1	1.4
Acute dilatation of stomach	1	1.4
	<hr/> 69	

The high frequency of peritonitis after the operations for fibroids in this series may be explained partly by the presence of extensive pelvic inflammatory lesions which were frequently associated with the fibroids, especially in the negroes. Furthermore, many of the fibroid masses were unusually large, many were adherent to the bowel and bladder, some were intraligamentous, and a few protruded into the vagina. In 21 of the 69 cases the appendix was removed, and how much of a factor this was in causing some of the deaths, it is difficult to say.

Embolism occurred in 9 of the fibroid cases, and whereas only 69 of the 213 (32.4 per cent) patients who died had fibroids, 9 of the 18 deaths from embolism (50 per cent) occurred in the fibroid series.

Postoperative hemorrhage and shock are placed together because it was difficult to tell when one or the other was responsible for the death. Part of this mortality was due to faulty technic and part to the anemic condition and other abnormalities of some of these patients.

Myocardial failure was responsible for one-tenth of the deaths in the fibroid group. This is not unexpected when we recall that many patients with large fibroids have some affliction of the cardiac musculature. The remaining deaths in the fibroid group require no special explanation.

There were 65 deaths following operations for pelvic inflammations. Most of these infections were due to gonorrhea, but some were due to tuberculosis and others were puerperal in origin. The operations for these 65 cases are listed in Table VII.

TABLE VII. OPERATIONS FOR THE 65 INFLAMMATORY CASES

TYPE OF OPERATION	NUMBER
Defundation, bilateral salpingectomy	16
Abdominal supracervical hysterectomy, bilateral salpingectomy, unilateral oophorectomy	11
Bilateral salpingectomy, unilateral oophorectomy	9
Posterior colpotomy	8
Bilateral salpingectomy	6
Abdominal supracervical hysterectomy, bilateral salpingo-oophorectomy	4
Abdominal panhysterectomy, bilateral salpingo-oophorectomy	4
Unilateral salpingo-oophorectomy	4
Exploratory laparotomy	3
	65

The cause of death in these 65 cases is shown in Table VIII.

TABLE VIII. CAUSE OF DEATH IN THE INFLAMMATORY CASES

CAUSE OF DEATH	NUMBER	PER CENT
Peritonitis	40	61.5
Hemorrhage and shock	14	21.5
Pneumonia	6	9.2
Embolism	2	3.1
Myocardial failure	1	1.5
Septicemia	1	1.5
Cachexia	1	1.5
	65	

It is not surprising to find that the majority of the fatalities were due to peritonitis, for in most of the cases in this group, a mild or severe degree of peritonitis had been present before operation. Of course, in the large proportion of the cases, the peritonitis was not an active one, but in a few cases there was evidence of active inflammation in spite of long rest in bed to overcome this.

In this group of 65 operations the appendix was removed 31 times. Undoubtedly in some of these cases where an appendectomy was performed, this operation played a rôle in leading to a fatal issue.

Hemorrhage and shock were responsible for 21.5 per cent of the deaths in the inflammatory group in contrast to 11.6 per cent in the fibroid cases. This may be due to the prolonged operations sometimes necessary in cases with extensive inflammation and also to the large exposed raw surfaces from which the blood oozing is sometimes controlled with difficulty. On the other hand embolism occurred in only 3.1 per cent of the inflammatory group in contrast to 13 per cent in the fibroid series. Likewise, myocardial failure accounted for 1.5 per cent of the former deaths in contrast to 10.1 per cent in the fibroid group.

The 31 malignancies consisted of:

1. Carcinomas of the cervix, the body of the uterus, the ovaries, the rectum, the sigmoid, the transverse colon, the cecum, the bladder, the vulva, and generalized carcinomatosis.

2. Sarcomas of the uterus, the broad ligament, the small intestine, and the vulva.

3. Teratomas of the ovary.

The eleven intestinal obstruction cases were treated by various means including, colostomy, ileostomy, resection of bowel and in one case only an exploratory operation and biopsy were done.

#### THE CAUSES OF DEATH IN THE 213 CASES

Almost half of all the fatalities were due to peritonitis and ileus, and these are listed together because whenever an ileus occurred peritonitis

TABLE IX. CAUSES OF DEATH FOR ALL CASES

CAUSE OF DEATH	NUMBER	PER CENT
Peritonitis and ileus	104	48.8
Hemorrhage and shock	35	16.4
Embolism	18	8.5
Pneumonia	18	8.5
Malignancy and cachexia	16	7.5
Myocardial failure	12	5.2
Uremia	2	0.9
Cerebral thrombosis	1	0.5
Acute dilatation of stomach	1	0.5
Septicemia	1	0.5
Pyelocystitis	1	0.5
Gas gangrene of pelvis	1	0.5
Pellagra	1	0.5
Encephalitis or meningitis	1	0.5
Pyemia	1	0.5
	213	

was also present. As mentioned previously, some of the patients had peritonitis before they were operated upon and died as a result of this rather than as the direct result of their operation. Several of the deaths from peritonitis were directly attributable to injuries which occurred to the bowel, bladder, and ureters during the operations. Two women in the peritonitis group had diabetes which was aggravated by their operation.

Hemorrhage and shock accounted for 16.4 per cent of all the fatalities. Usually the excessive loss of blood occurred during the operation, but in 12 cases there was serious postoperative bleeding. In most cases hemorrhage was the cause of shock but in others the causative factor of the shock was a prolonged operation, a long ether anesthesia or trauma during operation.

There were 18 cases of embolism (8.5 per cent) and half of these occurred after the 69 operations for uterine fibroids.

At least 95 per cent of the 6,022 operations were performed under ether anesthesia. Very few were done under spinal or direct infiltration anesthesia and a few patients had nitrous oxide and oxygen. Since there were 18 deaths from pneumonia in the entire series, the approximate incidence of this complication after ether anesthesia was almost 0.3 per cent. It is of course not maintained that the ether anesthesia was responsible for all the cases of pneumonia in this series. However, pneumonia is distinctly less frequent after the use of local anesthesia.

Malignancy and cachexia were usually associated, and they were put down as the cause of death when patients remained in the hospital a long time after operation and lost ground constantly without demonstrating any gross pathologic lesion other than the malignancy.

The remainder of the causes of death are self-explanatory.

#### COMPLICATIONS DURING OPERATION

The serious complications which occurred during operation are listed in Table X.

TABLE X. COMPLICATIONS DURING OPERATION

Ureter cut	4
Ureter ligated	1
Bladder torn	2
Sigmoid torn	2
Small intestines torn	2
Rectum torn	1
Hemorrhage during vaginal hysterectomy necessitating laparotomy	2

TABLE XI. SERIOUS POSTOPERATIVE COMPLICATIONS

Intraabdominal hemorrhage	12
Fecal fistula	7
Evisceration	5
Hemorrhage from vagina	1
Hemorrhage from cervix	1
Vesicoabdominal fistula	1
Bleeding from wound	1
Emphysema of abdominal wall	1

TABLE XII. INTERVAL BETWEEN OPERATION AND DEATH

Less than 24 hours	13	11-15 days	21
1 day	19	16-20 days	7
2 days	18	21-25 days	2
3 days	19	26-30 days	3
4 days	24	31-40 days	3
5 days	18	41-50 days	5
6 days	17	51-60 days	4
7 days	13	87 days	1
8 days	7	108 days	1
9 days	12		
10 days	6		213

Practically all the bladder and bowel injuries occurred in cases where there were extensive adhesions between inflamed adnexa and the bowel and bladder.

#### SUMMARY

In a series of 6,022 operations performed on the gynecologic service of the Cook County Hospital there were 213 deaths, an incidence of 3.5 per cent. All the patients were charity patients and about 50 per cent of them were negroes.

The mortality rates for the largest groups of operation were as follows: For the 747 abdominal supracervical hysterectomies, it was 0.8 per cent; for the 661 abdominal supracervical hysterectomies with bilateral salpingo-oophorectomies, it was 8.9 per cent; for the 350 abdominal panhysterectomies with removal of both adnexa, it was 4.3 per cent; for the 449 defundations with salpingectomy, it was 4 per cent; for the 201 abdominal panhysterectomies, it was 5.5 per cent; and for the 158 vaginal hysterectomies, it was 1.9 per cent.

The most frequent operative diagnoses in the fatal cases were fibroid uterus 69, salpingitis and pelvic inflammation 65, malignancy 31, ovarian cyst 13, and intestinal obstruction 11.

The commonest causes of death in the fibroid group were peritonitis 50.8 per cent; embolism 13 per cent, hemorrhage and shock 11.6 per cent, myocardial failure 10.1 per cent, and pneumonia 7.2 per cent. The chief causes of death for the inflammatory group were peritonitis 61.5 per cent, hemorrhage and shock 21.5 per cent, pneumonia 9.2 per cent, and embolism 3.1 per cent.

The most frequent causes of death for the entire series of 213 cases were as follows: peritonitis and ileus 48.8 per cent, hemorrhage and shock 16.4 per cent, embolism 8.5 per cent, pneumonia 8.5 per cent, malignancy and cachexia 7.5 per cent, and myocardial failure 5.2 per cent.

There were 14 serious complications during operation and 29 grave complications after operation.

#### CONCLUSIONS

1. The histories and progress notes should be much more complete than they are at present, and the attending physicians should add notes as well as the internes.

2. The patients should receive more preparation and have more tests made before operation. The sedimentation test should be employed routinely in inflammatory cases.

3. There should be more consultations with attending physicians in other services, especially the medical and urologic.

4. There should be more transfusions before operation, especially when there is to be an extensive operation.

5. Local anesthesia either by direct infiltration or by the spinal route should be used more frequently for selected cases.

6. No operation should be performed until the temperature has been normal at least ten days, except in rare cases.

7. The number of unnecessary appendectomies may be reduced with advantage.

8. Postoperative care should be supervised more closely.

9. An effort should be made to secure more autopsies.

185 NORTH WABASH AVENUE

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## POSTMENOPAUSAL BLEEDING\*

### A SURVEY OF 98 CONSECUTIVE CASES

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INASMUCH as bleeding from the vagina occurring after the menopause is frequently treated symptomatically and passed over as being of little or no significance, the authors deemed it of interest to analyze the etiologic factors responsible for this type of bleeding in all the case records from the gynecologic services at the Presbyterian and Cook County Hospitals for the year 1930. During that year 98 patients were admitted to these services with postmenopausal bleeding as part of, or as the entire symptom-complex.

The causes of this type of bleeding in the order of their frequency are as follows: carcinoma (67 cases), cervical polyps (8 cases), fibromyomas (7 cases), prolapse of the uterus (5 cases), senile vaginitis (3 cases), cervical erosion (3 cases), urethral caruncle (2 cases), fibrosis of the uterus (2 cases), and nonspecific ulcer of the vagina (1 case). Analyzing the carcinomas in this series we find that 51 were cervical, 11 were in the body of the uterus, 2 were on the vulva, 1 was in the vagina, 1 was in the ovary, and 1 was a zona granulosa tumor of the ovary. Of the fibromyomas, 4 patients had multiple fibroids while the other 3 had the single submucous type. Thus, in this series, 68.4 per cent of the cases were of

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a malignant nature and 31.6 per cent were benign. Table I gives an analysis of these figures together with the percentages of each condition as found.

TABLE I. DIAGNOSES AND PERCENTAGES

DIAGNOSIS	NUMBER OF CASES	PER CENT OF TOTAL
Carcinoma of the cervix	51	52.08
Carcinoma of the corpus	11	11.22
Carcinoma of the vagina	1	1.02
Carcinoma of the ovary	1	1.02
Carcinoma of the vulva	2	2.04
Zona granulosa tumor	1	1.02
Senile vaginitis	3	3.06
Urethral caruncle	2	2.04
Fibromyomas	7	7.14
Erosion of the cervix	3	3.06
Prolapse of the uterus	5	5.10
Polyps of the cervix	8	8.14
Ulcer of the vagina	1	1.02
Fibrosis of the uterus	2	2.04
Totals	98	100.0

*Age.*—The age incidence of bleeding after the menopause (Table II), reveals that the greatest number of the patients are between the ages of fifty and sixty. Of the 98 case records studied, 58 fall into this class, one

TABLE II. AGE INCIDENCE

AGE	NUMBER OF PATIENTS
48	1
49	0
50	6
51	6
52	6
53	5
54	4
55	5
56	6
57	3
58	4
59	5
60	8
61	4
62	5
63	4
64	2
65	2
66	3
67	1
68	2
69	2
70	2
71	2
72	2
73	1
74	2
75	2
76	2
77	1

TABLE III. NUMBER OF YEARS AFTER MENOPAUSE

YEARS IN MENOPAUSE	NUMBER
1	4
2	4
3	2
4	5
5	4
6	1
7	4
8	6
9	2
10	11
11	4
12	9
13	1
14	6
15	3
16	6
17	2
18	2
19	2
20	5
21	4
22	1
23	1
24	2
25	2
26	2
30	2
31	1



patient was under fifty, 27 were between the ages of sixty-one and seventy, while 12 were over seventy. The youngest patient in this series was forty-eight years of age, while the oldest was seventy-seven.

The number of years bleeding first occurred after the menopause was established, is shown in Table III. Bleeding may occur as early as the first year after the cessation of the menses and as long after that time as thirty-one years. The greatest numbers for any single year after the menopause occurred in the tenth and twelfth years, 11 and 9 respectively.

*Parity.*—The parity of the individuals studied is found in Table IV. This table is divided into two columns, one showing the relation of parity to carcinomas and the other to the nonmalignant conditions considered.

TABLE IV. RELATION OF PARITY TO POSTMENOPAUSAL BLEEDING

PARITY	CARCINOMATA	NONMALIGNANT
0	7	2
1	6	5
2	9	6
3	12	4
4	4	5
5	6	4
6	9	1
7	1	1
8	1	2
10	3	2
11	2	1
12	1	2
13	1	0
16	1	0

*Type of Bleeding.*—There were four types of bleeding complained of by the patients, namely: bloody stained leucorrhea, spotting, moderate in amount, and profuse with sizable hemorrhage and passage of large clots. Only four of the patients had a blood stained discharge, 38 had spotting, 28 had a moderate amount of bleeding, and 28 had profuse bleeding. Table V shows the relationship between the type of bleeding and the pathology present.

TABLE V. RELATION OF TYPE OF BLEEDING TO CAUSATIVE CONDITION

CONDITION	DISCHARGE	SPOTTING	MODERATE	PROFUSE
Carcinoma of cervix	2	16	17	16
Carcinoma of corpus	0	4	1	6
Carcinoma of vagina	0	1	0	0
Carcinoma of vulva	0	0	1	1
Carcinoma of ovary	0	0	1	0
Zona granulosa	0	0	1	0
Senile vaginitis	0	3	0	0
Urethral caruncle	0	1	1	0
Fibromyomas	0	4	0	3
Cervical erosion	0	3	0	0
Prolapse	1	2	1	1
Cervical polyp	1	3	4	0
Nonspecific ulcer	0	1	0	0
Fibrosis of uterus	0	0	1	1

*Duration of Bleeding.*—The great majority of the patients in this group presented themselves for treatment within one year of the time of the onset of the bleeding. Only eleven histories in the entire group stated that the patients had been bleeding for over one year, while 53 of them were seen within the first six months after the symptom showed itself. Table VI shows the length of time the various patients had bled before seeking specialized medical attention.

TABLE VI. DURATION OF BLEEDING BEFORE PRESENTATION IN HOSPITAL

ELAPSED TIME	NUMBER OF PATIENTS
1 month or less	12
2 months	10
3 months	9
4 months	6
5 months	5
6 months	11
7 months	5
8 months	2
9 months	2
10 months	1
11 months	2
1 year	22
2 years	9
3 years	2

*Menstrual Life.*—Although not entirely relevant to the subject in hand, we are able to tabulate some very interesting statistics on the age of onset of the menopause and the duration of menstrual life in this group of patients. We find that the earliest menopause in the series occurred at the age of thirty, while the latest cessation of menses took place at the age of fifty-seven. The largest number stopped menstruat-

TABLE VII. AGE AT MENOPAUSE

AGE AT MENOPAUSE	WHITE	COLORED
30	0	1
35	1	0
36	1	0
38	1	0
39	0	3
40	2	1
41	2	0
42	2	0
43	2	1
44	2	0
45	11	3
46	2	1
47	9	0
48	10	2
49	4	2
50	14	6
51	5	1
52	2	0
53	1	1
55	3	0
57	1	1

ing between the ages of forty-five and fifty-one. The shortest duration of menstrual life here encountered was seventeen years, while the longest was forty-three years. Of particular interest is the obstetric history of some of these patients. The patient who menstruated only seventeen years was a nulliparous individual, while the one who had an 18-year span of active menstrual life had had six children. The woman who menstruated through a period of forty-three years also had six children; one who menstruated for forty-one years had had one child; the three patients who menstruated forty years were para 1, 8, and 16, and finally the patient who had a thirty-nine year menstrual life was a nulligravida. Table VII shows the age at the onset of the menopause, and Table VIII shows the duration of menstrual life. In Table VII we have divided the white and the colored patients into separate columns in order that we might have a basis of comparison between the two races in regard to this particular subject. The average length of menstrual life as found in this series is 28.07 years.

TABLE VIII. DURATION OF MENSTRUAL LIFE

YEARS OF MENSTRUATION	NUMBER
17	1
18	1
20	1
21	1
24	2
25	3
26	1
27	2
28	1
29	5
30	4
31	3
32	11
33	6
34	7
35	6
36	13
37	6
38	7
39	1
40	3
41	1
43	1

Another interesting observation made in the review of these cases is the fact that one of the patients who presented herself with a carcinoma of the cervix had had a supracervical panhysterectomy for multiple fibroids just two years previous to the development of the symptoms from her carcinoma.

#### DISCUSSION

Causes of postmenopausal bleeding not actually encountered in this series but which must be looked for in a thorough examination of the

pelvis are senile endometritis, simple cystadenoma of the ovary, sarcoma of the ovary, torsion of the pedicle of an ovarian cyst, pyometra, foreign bodies in the vagina or uterus, and carcinoma of the fallopian tube.

The diagnosis of most of these conditions can readily be made by bimanual palpation and direct inspection of the vagina and cervix through a speculum. When neither of these procedures gives us a successful diagnosis, a diagnostic curettage with careful study of the recovered material is indicated. If this proves of no avail a posterior colpotomy incision can be made and the adnexal regions brought into view for direct inspection, because the zona granulosa tumor or early ovarian carcinomas which may be too small for palpatory detection, can, in this manner be determined. The type of bleeding present is of no value in the determination of the prevailing cause as we can see by Table V.

The idea that certain lesions of the uterus or ovary are capable of exciting cyclic endometrial activity after the menopause has been established is very doubtful. Some believe that the zona granulosa tumor of the ovary is capable of doing this, but the most likely cause of the bleeding when this condition is present is a coexisting carcinoma of the endometrium. Herd studied the ovaries of twenty patients who had postmenopausal cysts or carcinomas, and in only one instance did he find evidences of ovarian activity. That patient had a sarcoma of the endometrium as the probable cause of the bleeding.

In a large number of cases of postmenopausal bleeding, the exciting factor is constant irritation or contact, as is manifested in the bleeding from urethral caruncles, senile vaginitis, erosions of the cervix, cervical polyps, and foreign bodies in the vagina or cervix. As an added factor in cervical polyps or fibrosis of the uterus, arterial hypertension may be of significance. In the submucous fibroid or fibroid polyp, bleeding is due to a change in the capsule of the tumor or an ulceration in a congested part of the polyp. In malignancy of the cervix or corpus uteri, the ulceration caused by direct invasion of the malignant cells with secondary infection is the factor responsible for the bleeding. Large ovarian cysts, malignant or benign, or a moderate-sized cyst with twisting of its pedicle produce bleeding by causing a marked generalized pelvic congestion. Our conception of the cause of the bleeding in the rare zona granulosa tumor of the ovary is stated in the preceding paragraph.

#### SUMMARY

1. Inasmuch as 68.4 per cent of the patients in our series with postmenopausal bleeding had conditions of a malignant nature, the axiom, "All cases of postmenopausal bleeding should be considered as malignancies until proved otherwise," is very significant.

2. The possible causes of postmenopausal bleeding are: carcinoma of the cervix, carcinoma of the corpus uteri, carcinoma of the vagina, carcinoma of the vulva, carcinoma of the ovary, zona granulosa tumor of

the ovary, senile vaginitis, urethral caruncle, fibroids of the uterus, cervical erosions, prolapse of the uterus, cervical polyps, fibrosis uteri, nonspecific ulceration of the vagina, senile endometritis, sarcoma of the ovary, large cysts of the ovary, pyometra, twisting of the pedicle of an ovarian cyst, foreign bodies in the vagina or uterus, and carcinoma of the fallopian tube.

3. Once the menopause has been definitely established (no menses for a period of six months to one year) all bleeding from the genitals should be considered as abnormal.

4. There is no apparent relationship between the type or amount of bleeding and the seriousness of the existing condition.

5. Parity, length of time in the menopause, and duration of active menstrual life are of no particular value as diagnostic aids.

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310 SOUTH MICHIGAN AVENUE.

## COMPLETE INVERSION OF THE UTERUS AND CERVIX\*

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MRS. G. S. (Hist. No. 38060.) Color, white, aged twenty-two, occupation, housewife, entered the hospital March 4, 1931. Chief complaint: prolapse of uterus associated with bleeding. Present illness: On May 5, 1930 patient gave birth to her third child after a full-term normal pregnancy and normal labor. The third stage of labor was unduly prolonged. Patient does not believe she received any medication to expedite labor. Her attending physician exerted strong traction on the cord which produced a sharp pain in the lower left quadrant. He scraped the placenta from the uterus manually and told her that the womb had slipped out of the vagina. An unsuccessful attempt was then made to replace the womb which was associated with a moderate loss of blood but no loss of consciousness. She was kept in bed in the Trendelenburg posture for three weeks and then lay in the lateral position for seven weeks longer. Bleeding was not marked throughout this time. She gives no history of a severe febrile course.

At the end of eleven weeks she attempted to get out of bed and noticed a reddish globular mass extruding from the vagina for a distance of two or three inches. On attempting to walk there was a fairly profuse bleeding. Her physician gave her a sort of truss which was designed to keep the uterus within the vagina but she was unable to wear it on account of tenderness. Her condition remained the same for the next five months. She was forced to remain in bed most of the time because of

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marked vaginal bleeding upon even slight exertion. She became very weak and dizzy but has never lost consciousness. Constant oozing continued until admission to the hospital. Her past history and menstrual history are of no importance or interest. She had been married for four years. Husband living and well. There have been three pregnancies and two living children. The last baby died at three months of age of dysentery. Family history is of no importance.

The patient was fairly well developed but poorly nourished. She was not acutely ill or uncomfortable. Skin was pale but warm and dry. Mucous membranes showed marked pallor. She was moderately intelligent and cooperative.

The physical examination was essentially negative except a systolic blowing over the precordium, loudest in the pulmonic area. Blood pressure 128/78; pulse soft and equal, rate 120.



Fig. 1.—Complete inversion of uterus and cervix. One tube and ovary were removed; the other appendage was left in situ.

Pelvic examination, external genitals were negative, vaginal outlet moderately relaxed. Filling the vagina was a purplish pear shaped mass seemingly covered with mucous membrane which bled profusely on manipulation. On bimanual examination the uterus could not be palpated in the pelvis, but there could be felt a cup-shaped depression beneath the symphysis. Traction on the tumor caused it to be pulled outside of the vaginal outlet. It seemed to be a complete inversion of the uterus. The openings of the fallopian tubes could not be demonstrated.

Clinical laboratory: urine negative; R.B.C. 2,630,000; W.B.C. 7,050; Hg 42 per cent (Sahli); Wassermann and Kahn negative; Phenolsulphonephthalein output 50 per cent the first hour, second hour specimen not collected; sedimentation time sixty minutes; temperature on admission 99.6; pulse 120; respiration 20.

Preoperative diagnosis: inversion of the uterus, complete, and secondary anemia.

Under gas-oxygen anesthesia an unsuccessful attempt was made to reduce the in-

version. During the next week three blood transfusions were given which finally brought the R.B.C. to 5,000,000; Hg 78 (Sahli).

On March 18, 1931 a vaginal hysterectomy and salpingo-oophorectomy, unilateral, were carried out, which was ten months and thirteen days after she was delivered. Her postoperative course was uneventful. The patient was discharged in good condition April 2, 1931.

Microscopic examination of the specimen showed the endometrium contained only one to two glands per high power field. The epithelium was indistinct, no cellular detail in glands or stroma. Final diagnosis: beginning necrosis of the endometrium.

2112 WEST END AVENUE

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## CARCINOMA AND SARCOMA COEXISTING IN THE SAME UTERUS\*

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THE development of both of these tumors in the same uterus is exceedingly rare. Ewing reports ten cases in which a sarcoma and carcinoma were found in the same uterus. Most of these were polypoid sarcoma associated with diffuse adenocarcinoma. The case which I have to report is of this same type. In a complete review of the literature in 1929, Newell found only twenty cases in which a sarcoma and a carcinoma were coexisting in the same uterus.

*Clinical History.*—Mrs. G. G. R., aged fifty-six years, was first seen January 27, 1930, complaining of vaginal bleeding. The family history was irrelevant. The patient had had four term pregnancies, one child died with rheumatic fever and three children are living and well. There were no miscarriages. Her menstrual periods began at the age of thirteen years and were normal up to the menopause which was delayed until the age of fifty. Since the menopause she has had slight periods of bleeding about once a year lasting a few days. During the last two years she had noticed considerable watery discharge which was at times blood tinged. During the last two months there had been definite vaginal bleeding, and ten days before I first saw her, she passed a piece of tissue, which was associated with a severe hemorrhage. This was sent by her physician for examination and found to be a broad spindle cell sarcoma. She did not know her average weight, but weighed 218 pounds on my office scales. She had noticed some loss of appetite. There had been no abdominal pain.

The physical examination was essentially negative excepting for a moderate elevation of blood pressure to 150/90 and the pelvic findings. The abdominal wall was so fat and pendulous that nothing could be determined by palpation. Vaginal examination revealed a slightly hypertrophied cervix with a small erosion on the posterior lip. This erosion did not bleed and did not have the appearance of being malignant. The uterus was uniformly enlarged to about the size of a two months' pregnancy and was moderately movable in the pelvis. The adnexa could not be palpated. There was a thin bloody discharge present at the time of the examination.

The laboratory examination showed a red blood count of 4,170,000, hemoglobin 72 per cent, and a white blood count of 7,900. The urine was negative.

*Operation.*—January 31, 1930. Abdominal hysterectomy, bilateral salpingo-oophorectomy. A midline incision was made from symphysis to umbilicus. Upon opening the abdominal cavity the uterus was found to be uniformly enlarged to about

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\*Read before the Central Association of Obstetricians and Gynecologists, Chicago, October 29 and 30, 1931.

the size of a two months' pregnancy. There had been a very marked old inflammatory process involving the left adnexa and parametrium, making it difficult to lift the uterus up out of the pelvis even after the adhesions were freed. We, of course, started the operation with the intentions of doing a panhysterectomy, but with the mechanical difficulties of an extremely fat abdominal wall, a deep pelvis, and dense adhesions, together with the fact that the patient did not seem to be standing the operation well, we decided to amputate the uterus, leaving as little of the cervix as possible, and closed the abdomen. In other words, I felt that I would rather have the patient recover from the operation and take a chance on a recurrence in the cervical stump, than to have the complete specimen and have the patient die from the operation. Accordingly the uterus with both tubes and ovaries was removed, the uterus being amputated below the level of the internal os. The round and infundibulopelvic ligaments were sutured into the cervical stump and the bladder peritoneum was used to cover the raw surfaces. The abdomen was closed, without drainage, in the usual manner.

The postoperative course was fairly smooth and the patient was out of bed on her fourteenth day.

*Subsequent Course.*—The patient had four deep x-ray treatments over the pelvis during the following month. I have examined this patient several times since her operation and have found the cervix and pelvis free from any evidence of recurrence. The last examination was made twenty-one months following the operation. The patient was feeling well, in good health, and weighed 234 pounds, which was a gain of sixteen pounds above her weight before the operation.

*Pathologic Examination.*—Gross appearance: The uterus which was amputated supracervically measured 8 by 8 cm. The lumen was very much dilated and a polyp with a base of 2.5 cm. and a height of 4.5 cm. was protruding from the lower half of the corpus. The consistency of the polyp was soft. It was brain-like in color.

Microscopic findings. The polyp was composed of strands of large short oval cells. They had different size and staining quality of the vesicular nucleus. There were some mitotic figures. The endometrium was invaded by an adenocarcinoma with long branching glands lined with atypical dark cells in several rows. The adenocarcinoma was invading deeply into the myometrium. Sections from the cut surface of the cervix showed a narrow area of normal cervical glands and muscle tissue not invaded by carcinomatous tissue.

*Pathologic Diagnosis.*—Sarcomatous polyp. Adenocarcinoma of the body of the uterus.

One can easily see how difficult it is to make an accurate diagnosis when two malignancies spring from the interior of the uterine cavity and encroach upon each other in such a way that the cells may lose their characteristics. It is not so difficult however, in the case reported, because sections are found showing each type of malignancy distinct and separate from the other.

The author wishes to take this opportunity to express his indebtedness and thanks to Dr. C. A. Helwig, pathologist of the St. Francis Hospital, for the pathologic report.  
902 BROWN BUILDING.



# A CASE OF ANAPLASTIC CARCINOMA OF THE BODY OF THE UTERUS\*

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IT IS the purpose of this communication to record the clinical and pathologic observations in a case of anaplastic carcinoma of the body of the uterus, and to correlate these findings with certain previous reports describing this type of tumor.

*Case Report.*—The patient was a white married woman, aged forty years. She had no children. There had been two pregnancies seventeen years and eighteen years previously, both of which terminated in spontaneous eight weeks' abortions.

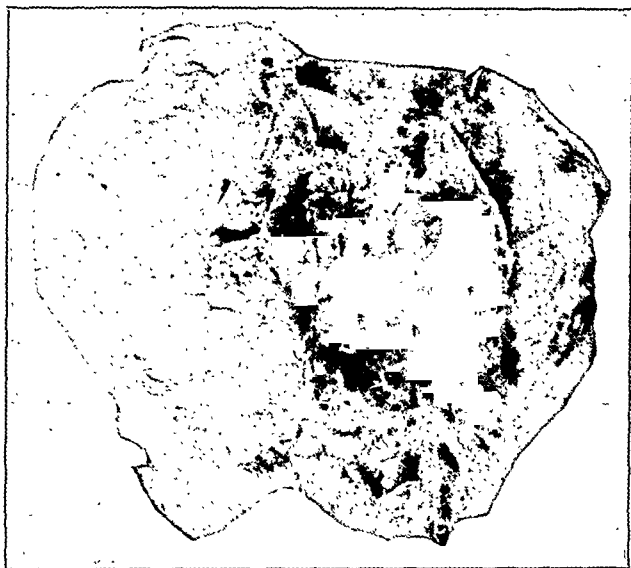


Fig. 1.—Gross specimen showing necrotic, friable tumor filling uterine cavity and several intramural myomas.

Menstruation began at the age of twelve years. The periods were of the twenty-eight day type and regular. The menstrual flow had always been somewhat profuse and the duration seven to ten days. There was no dysmenorrhea and no intermenstrual bleeding. On admission the patient stated that she had been entirely well until three months previously when she developed anorexia and began to lose weight to the extent of fifteen pounds in three months. She also suffered with increasing constipation and progressive weakness. The last menstrual period began four weeks before admission, was accompanied by marked dysmenorrhea, and the menstrual flow was unusually profuse and prolonged.

On physical examination it was found that the patient was pale, thin, and undernourished. The abdomen was relaxed and pendulous. A firm, irregular mass filled the pelvis, and extended to within 3 cm. of the umbilicus. On vaginal examination it was found that there was moderate vaginal bleeding. The cervix was intact and merged into a firm, irregular, nodular, fixed mass in the position of the uterus, and

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filling the entire pelvis. There was definite nodularity in the culdesac. Examination of the blood showed a pronounced secondary anemia: (R.B.C. 2,400,000; W.B.C. 10,850; Hb. 65 per cent). The sedimentation test showed a ten minute rate. The preoperative clinical diagnosis was multiple myomas complicated by sarcoma.

After a direct transfusion of 500 c.c. of blood, the abdomen was opened in the midline. The uterus was found to be the size of a four months' gestation. Several myomas were plainly visible in its walls. A supracervical hysterectomy was performed as a palliative measure. The patient was discharged five weeks after admission in fair condition. She died two months after operation with symptoms suspicious of pulmonary and hepatic metastases.

*Pathologic Examination.*—The uterus was enlarged. There were several intramural and subserous myomas varying between one and 3 cm. in diameter. Upon opening the uterus the cavity was found largely filled with, and somewhat distended by, a soft, friable, seminecrotic tumor arising in the endometrium. Some of the necrotic debris lay free in the uterine cavity.

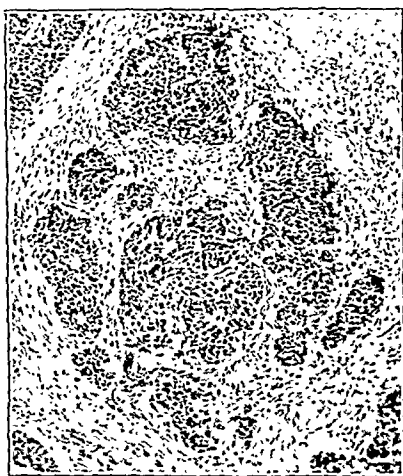


Fig. 2



Fig. 3

Fig. 2.—Photomicrograph showing diffuse growth of anaplastic carcinoma. The cells are small and there is complete loss of polarity.

Fig. 3.—Photomicrograph showing polyhedral and small spindle cells surrounding a blood vessel, simulating the morphologic structure of a peritheliomatous growth.

*Histologic Examination.*—Histologic examination showed a highly cellular and malignant tumor, probably of epithelial origin. At no point was there any evidence of glandular formation. The growth was diffuse. The individual cells exhibited all the morphologic signs of anaplasia. There was marked variation in size and shape of cells and hyperchromatism of nuclei with numerous atypical mitoses throughout. The tumor cells were round, polyhedral and occasionally spindle-shaped. In some areas the cells were grouped around blood vessels giving a peritheliomatous appearance. There were several foci of giant cells of the foreign body type with highly atypical nuclei and numerous mitoses. There was no evidence of invasion of blood vessels by tumor cells. There were numerous necrotic and seminecrotic foci.

#### DISCUSSION

Whatever doubts may exist concerning the precise relationship between the histologic structure of tumors and their prognosis, it appears to be definitely established that the highly undifferentiated anaplastic carcinomas are usually the most malignant tumors that are encountered.

The unfavorable prognosis of highly anaplastic carcinomas following surgical procedures has been demonstrated in cases affecting the lip (Broders<sup>1</sup>); the tongue, tonsil, pharynx and larynx (Ewing<sup>2</sup>); the cervix (Broders, Martzloff,<sup>3</sup> Schmitz,<sup>4</sup> Healy and Cutler<sup>5</sup>); and the body of the uterus (Mahle,<sup>6</sup> Lindsay,<sup>7</sup> Norris and Vogt,<sup>8</sup> Healy and Cutler<sup>9</sup>).

In 1923 Mahle reported 186 cases of fundus carcinoma treated in the Mayo Clinic and concluded that a definite relationship existed between the histologic structure and the end-result after hysterectomy. He noted that in Grade I, the most differentiated form, no deaths occurred. Whereas in Grade IV (the anaplastic type) in which there was complete loss of differentiation, every patient died. Lindsay in 1927 analyzed a large series of cases from the Memorial Hospital and the New York Hospital and confirmed these results.

In 1930 Healy and Cutler reported 100 cases of carcinoma of the fundus uteri from the Memorial Hospital, New York. Twelve per cent were found to belong to the anaplastic type of carcinoma. Of these, six died and six lived over three years.



Fig. 4

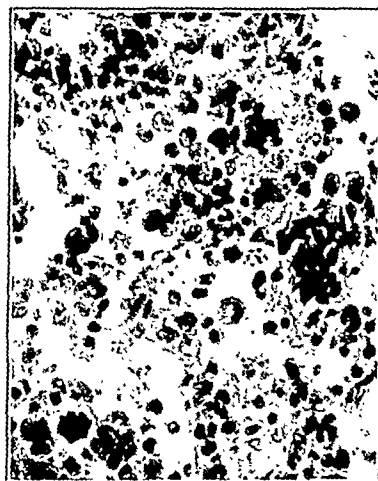


Fig. 5

Fig. 4.—Masses of giant cells with atypical, hyperchromatic nuclei. Many cells are in a state of mitosis.

Fig. 5.—High power photomicrograph showing the atypical and very active giant cells.

One patient was cured by hysterectomy, one by removal of a pedunculated growth followed by intrauterine radiation. Four patients are well after preoperative radiation followed by hysterectomy. In one case a very large tumor responded rapidly and almost disappeared entirely after radiation therapy. The patient remained well five years, after which hysterectomy was performed for suspected pyometra. On microscopic examination only nuclear remnants of tumor cells could be detected. There was no viable tissue to be demonstrated.

#### CONCLUSIONS

1. Anaplastic carcinoma of the body of the uterus, which forms about 12 per cent of all carcinomas affecting the uterus, is the most malignant form of fundus carcinoma. It is at the same time the most radiosensitive.

2. The prognosis in this group of cases is extremely unfavorable under all circumstances.

3. In view of their high degree of potential malignancy and their radiosensitivity, preoperative radiation is urgently indicated in all cases.

4. The method of choice in the treatment of anaplastic carcinoma of the uterus is preoperative radiation followed by hysterectomy in the operable group and radiation alone in the inoperable group.

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104 SOUTH MICHIGAN AVENUE.

## URINARY TRACT CHANGES DURING LATE PREGNANCY AND EARLY PUERPERIUM\*

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THE anatomic changes which take place in the kidneys and ureters during pregnancy and the late puerperium are well known. Hofbauer<sup>10</sup> has demonstrated the histologic changes and Duncan and Seng<sup>4</sup> have shown by retrograde pyelography the gross changes occurring in the urinary tract during pregnancy and the puerperium from the ninth to the twenty-fifth day postpartum, but very little is known about the events of the ten day period immediately following delivery. The introduction of intravenous urography by means of contrast material excreted through the kidneys has opened a safe method of approach to this problem.

Our investigations were directed at this immediate puerperal period, and the contrast material used was the sodium salt of iodo-methane-sulphonic acid, known in Germany as "Abrodil" and in this country as "Skiodan." The chemical formula of this compound is  $\text{ICH}_2\text{SO}_3\text{Na}$ . Bronner, Hecht and Schueller<sup>2, 3</sup> studied the chemical and physiologic reactions of the drug and showed that it may be employed safely for pyelographic studies repeated as often as every twenty-four hours.

## METHOD

The subjects included 41 normal pregnant women, 20 primiparas and 21 multiparas. Of the latter, 8 had had one, 7 two, and 6 three or more children. The age of the patients ranged from sixteen to twenty-eight years for the primiparas, and sixteen to thirty-six for the multiparas. In order to establish an index of the amount and frequency of pelvic and ureteral dilatations, and as a basis for judging postpartum changes, the first films were made during late pregnancy, and repeated exposures, usually three or four, were obtained during the ten to four-

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teen days following delivery. Stereoroentgenograms were taken in all cases to avoid the objection that a single film, if taken during a peristaltic contraction, might not represent the true size of the ureter. Obviously the antepartum pictures were uniformly better than those taken postpartum because of the marked urinary stasis present during late gestation.

#### ANTEPARTUM RESULTS

Seventy-five per cent of the antepartum plates were taken less than thirty days before delivery, although the range was from one to sixty-

TABLE I. SHOWING DEGREE OF DILATATION FOR PRIMIPARAS  
(Number of Cases, 20)

DILATA- TION	CALYX				PELVIS				URETER			
	RIGHT		LEFT		RIGHT*		LEFT		RIGHT		LEFT	
	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%
Marked	14	70	4	20	10	50	2	10	9	45	2	10
Moderate	5	25	6	30	9	45	8	40	7	35	10	50
Slight	1	05	7	35	1	05	10	50	4	20	6	30
None	0	00	3	15	0	00	0	00	0	00	2	10
Dilatation all grades	20	100	17	85	20	100	20	100	20	100	18	90

TABLE II. SHOWING DEGREE OF DILATATION FOR MULTIPARAS  
(Number of Cases, 21)

DILATA- TION	CALYX				PELVIS				URETER			
	RIGHT		LEFT		RIGHT		LEFT		RIGHT		LEFT	
	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%
Marked	11	52	2	09.5	9	43	2	09.5	10	48	2	09.5
Moderate	9	43	10	48	11	52	11	52	6	28.5	12	57
Slight	1	05	3	14	1	05	4	19	5	24	6	28.5
None	0	00	5	24	0	00	3	14	0	00	1	05
Dilatation all grades	21	100	15	71	21	100	17	81	21	100	20	95

TABLE III. SHOWING COMPARISON BETWEEN PRIMIPARAS AND MULTIPARAS  
(Given in Percentage)

	RIGHT						LEFT					
	CALYX		PELVIS		URETER		CALYX		PELVIS		URETER	
	PRIM.	MULT.	PRIM.	MULT.	PRIM.	MULT.	PRIM.	MULT.	PRIM.	MULT.	PRIM.	MULT.
Marked	70	52	50	43	45	48	20	09.5	10	09.5	10	09.5
Moderate	25	43	45	52	35	28	30	48	40	52	50	57
Slight	05	05	05	05	20	24	35	14	50	19	30	28.5
None	00	00	00	00	00	00	15	24	00	14	10	05
Not readable								05		05		
All grades	100	100	100	100	100	100	85	71	100	81	90	95

five days before the onset of labor. In general only one antepartum reading was taken, but in five cases a second exposure was made to obtain a better film. Each roentgenogram was read independently and the readings coincided except for occasional slight differences in expressing the degree of dilatation. Tables I, II, and III indicate that in all primiparas and multiparas there is some degree of dilatation of the right side while on the left side the percentage of patients showing dilatation is high. These figures are in accord with the findings of Duncan and Seng,<sup>4</sup> except that we find a larger number of left sided dilatations.

#### POSTPARTUM INVOLUTION OF THE URINARY TRACT

The authors just quoted found that involution takes place within nine to twenty-five days in a minority of the cases although the majority had not completed involution at the time of the cystoscopy. In two instances dilatation persisted for twenty-one months and nine years respectively.

TABLE IV. COMPARISON OF DEGREE OF DILATATION ANTEPARTUM AND ONE DAY POSTPARTUM

CASE NUM- BER	CALYX				PELVIS				URETER			
	RIGHT		LEFT		RIGHT		LEFT		RIGHT		LEFT	
	AP	PP	AP	PP	AP	PP	AP	PP	AP	PP	AP	PP
1	2	0	0	2	2	1	1	2	1	0	0	0
2*	2	0	0	0	2	1	1	1	1	2	2	2
12	3	2	2	2	2	2	2	1	2	2	1	1
20	3	0	0	0	3	1	1	1	1	0	0	1
21	3	3	1	0	3	x	2	1	3	x	2	0
25	3	3	3	1	2	2	3	0	2	3	3	1
29*	1	0	1	1	1	0	1	1	1	1	1	1
31	3	1	2	0	2	2	2	1	3	1	2	2

3, severe dilatation; 2, moderate dilatation; 1, slight dilatation; 0, no dilatation; x, unable to read; \*, febrile cases.

We were impressed by the rapidity with which involution took place immediately following delivery in eight patients whom we happened to study one day postpartum. Except for Cases 2 and 29 with febrile reactions during the puerperium, there was a marked reduction in the extent of the dilatation within twenty-four hours. In these eight patients the right calices showed definite reduction in 75 per cent, the left calices in 38 per cent, the right pelvis and left pelvis each in 50 per cent, the

TABLE V. SHOWING PERCENTAGES OF RETURN TO NORMAL IN 17 CASES IN WHICH READINGS WERE TAKEN 9, 10, OR 11 DAYS POSTPARTUM  
(Number of cases, 17)

CALYX				PELVIS				URETER			
NUMBER		PER CENT		NUMBER		PER CENT		NUMBER		PER CENT	
R	L	R	L	R	L	R	L	R	L	R	L
11	8	65	47	7	7	41	41	10	11	59	65

right ureter in 38 per cent, the left ureter in 25 per cent. Complete involution was observed in the calices in 50 per cent of the cases, in the pelves in 12.5 per cent, and in the ureters in 35 per cent.

Table V shows percentages of return to normal in 17 patients who were studied nine, ten, or eleven days postpartum. It will be seen that the pelves were considerably slower in their involution than were either

TABLE V-A. THE SAME TABLE WHEN FIVE PATIENTS HAVING INFECTION, OR URETERAL ANOMALY, WERE REMOVED FROM THE GROUP  
(Number of cases, 12)

CALYX				PELVIS				URETER			
NUMBER		PER CENT		NUMBER		PER CENT		NUMBER		PER CENT	
R	L	R	L	R	L	R	L	R	L	R	L
10	7	92	67	7	7	58	58	10	10	83	91

the calices or the ureters. This group, however, included 5 patients who might be considered abnormal because of infection or ureteral anomaly. Table V-A shows how much more uniform the return to normal becomes when these 5 patients are excluded.

TABLE VI. ALL CASES, SHOWING NUMBER AND PERCENTAGE WHICH SHOWED SOME REDUCTION AT FINAL READING  
(Number of cases, 41)

CALYX				PELVIS				URETER			
RIGHT		LEFT		RIGHT		LEFT		RIGHT		LEFT	
NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%
38	93	25	61	37	90	28	68	32	78	31	76

TABLE VI-A. THE SAME TABLE WHEN CASES HAVING NO ANTEPARTUM OR POSTPARTUM DILATATION AND THOSE WHERE READINGS COULD NOT BE MADE WERE ELIMINATED

CALYX				PELVIS				URETER			
RIGHT		LEFT		RIGHT		LEFT		RIGHT		LEFT	
NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%
38	95	25	100	37	93	28	85	32	82	31	83

From Table VI, it appears that at the time of the final reading (six to sixteen days postpartum) all dilatation had disappeared in a considerable percentage of the cases. Exclusion of those patients in whom there was no antepartum distention, and of those with unsatisfactory final films, increases the incidence of complete involution. (Table VI-A.)

Our results offer no conclusive evidence as to relative rapidity of involution in primiparas and multiparas, but wherever there is an appreciable difference, it favors the latter. Before, or at the end of the

twelfth day postpartum, there was a slightly higher percentage of primiparas than multiparas showing some residual dilatation of the urinary tract. And, except for the left pelvis, the primiparas presented a higher percentage of marked dilatation than did the multiparas at this stage of the puerperium. This quite agrees with the demonstration that extreme antepartum dilatation is more common among primiparous patients than in the parous. However, it is possible that the apparent tardiness in primiparas was due to the fact that the degree of dilatation had been more marked originally. With this possibility in mind, all patients who had shown marked antepartum dilatation were studied again. The left side was ignored because of the small size of the group. Twelve primiparas and 10 multiparas showed marked antepartum dilatation of the right calices while eight of each group showed similar dilatation in

TABLE VII. SHOWING DEGREES OF DILATATION OBSERVED IN PRIMIPARAS AND MULTIPARAS AT OR BEFORE THE END OF THE PUERPERIUM  
(Given in Percentage)  
(Number of Cases, 16 Primiparas; 19 Multiparas)

	CALYX				PELVIS				URETER			
	RIGHT		LEFT		RIGHT		LEFT		RIGHT		LEFT	
	PRIM.	MULT.	PRIM.	MULT.	PRIM.	MULT.	PRIM.	MULT.	PRIM.	MULT.	PRIM.	MULT.
Moderate	25	10.5	00	05	25	10.5	06	21	25	16	12.5	05
Slight	19	26	31	21	44	42	44	26	25	31	19	16
None	56	58	50	68	31	42	44	48	50	48	62.5	79
Not read- able	00	05	19	05	00	05	06	05	00	05	06	00
All grades	44	37	31	26	69	53	50	48	56	37	31	16

TABLE VII-A. COMPARISON OF DEGREE OF DILATATION BETWEEN PRIMIPARAS AND MULTIPARAS AT END OF PUERPERIUM IN CASES WHICH SHOWED MARKED ANTEPARTUM DILATATION

	RIGHT CALYX				RIGHT PELVIS				RIGHT URETER			
	NUMBER		PER CENT		NUMBER		PER CENT		NUMBER		PER CENT	
Number of cases	12	10			8	8			8	8		
Dilatation shown by last plate	Prim.	Mult.	Prim.	Mult.	Prim.	Mult.	Prim.	Mult.	Prim.	Mult.	Prim.	Mult.
Moderate	3	2	25	20	3	3	37.5	37.5	3	4	37.5	50
Slight	3	3	25	30	5	3	62.5	37.5	4	2	50	25
All grades			50	50			100	75			87.5	75

the pelves and ureters. Table VII-A compares these groups. Again there is a suggestion that the primiparas exhibited a slightly greater tardiness in return to normal. However, further work is necessary to substantiate these tentative findings. (It should be noted that there





Fig. 1.—Para v. seventeen days antepartum.



Fig. 2.—Three days postpartum. Another plate taken six days postpartum showed essentially the same picture.

These plates show the typical course of involution in normal patients.

are no marked dilatations postpartum in these groups, for all of these patients had some degree of involution.)

#### INVOLUTION IN THE PRESENCE OF INFECTION

Five of the patients in the series had chronic gonorrhea, and it is interesting to note that involution was noticeably slower in this group. Five other patients had a definite low grade postpartum intrauterine infection. Two of these infections followed operative labors, cesarean sec-

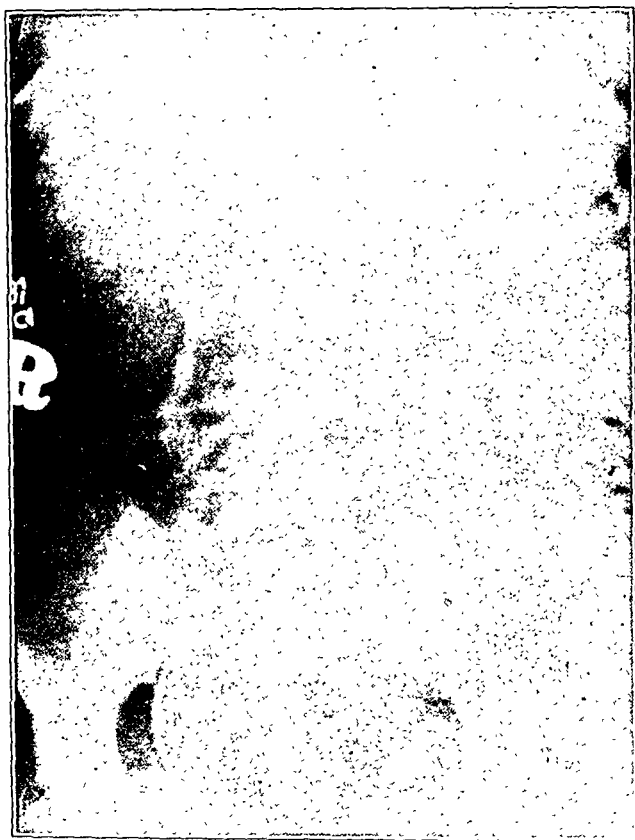


Fig. 3.—Primipara, twelve days antepartum. Note dilatation of ureters and kidney pelvises.

tion, and low forceps, and three developed after spontaneous labor, one of which lasted forty-seven hours and thirty-four minutes.

This last patient was an eighteen-year-old primipara with normal pelvis and a normal baby lying in L.O.A. The antepartum plate (Fig. 3) was taken twelve days prior to the onset of labor, which was spontaneous following medical induction. Although the first stage was prolonged, the second stage lasted but one hour and thirty-two minutes. The temperature rose slightly on the third postpartum day and went above  $100.4^{\circ}$  F. on the fourth and fifth days. At this time the patient complained of pain in the left flank although a catheterized specimen of urine showed no pus cells. The next two pictures were taken (Fig. 4) one day postpartum when the patient was afebrile and on the morning of the fourth day (Fig. 5) when she was outspokenly febrile.

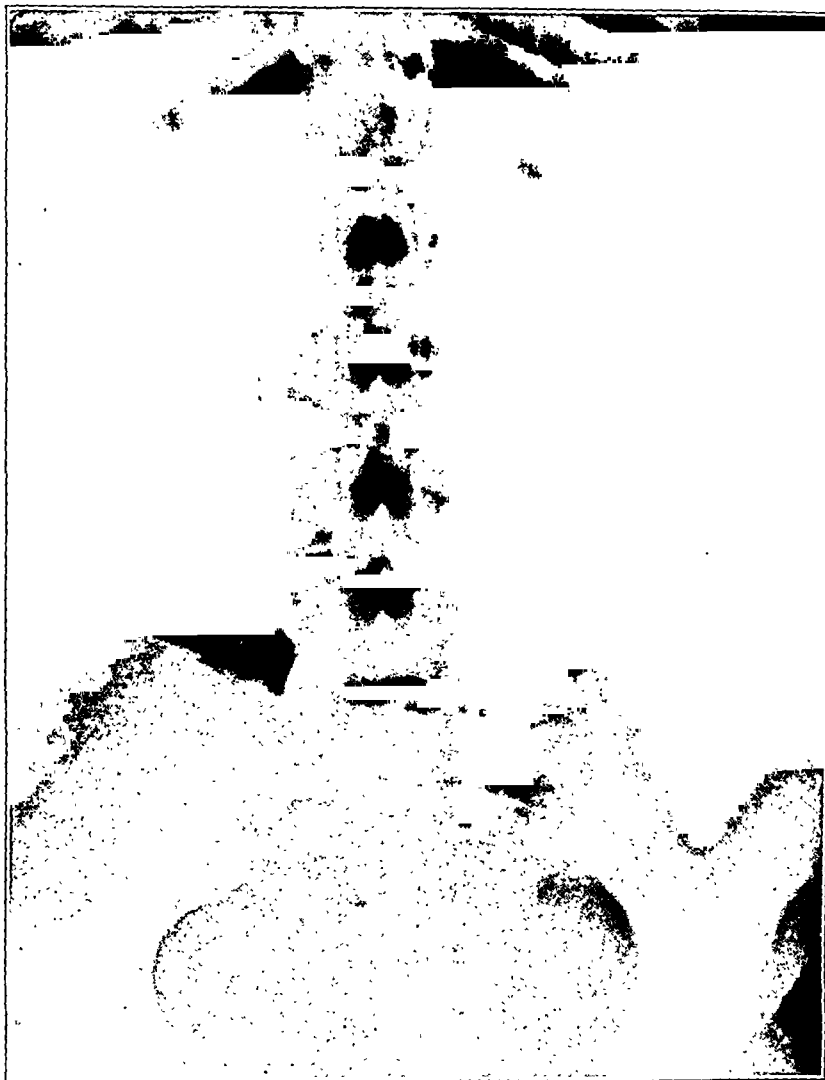


Fig. 4.—One day postpartum, afebrile. Compare dilatation of ureters and pelvis as shown in Fig. 3. Note marked decrease in size.

This series of pictures is typical of the findings in the other four febrile patients. Tables VIII and VIII-A give a composite picture of the tardiness with which the involution of the urinary tract progressed in

TABLE VIII. SHOWING PERCENTAGES OF RETURN TO NORMAL IN PATIENTS WITH DEFINITE POSTPARTUM INFECTION

(Number of Cases, 5)

CALYX				PELVIS				URETER			
NUMBER		PER CENT		NUMBER		PER CENT		NUMBER		PER CENT	
R	L	R	L	R	L	R	L	R	L	R	L
2	1	40	20	1	1	20	20	1	0	20	00.0

TABLE VIII-A. SHOWING PERCENTAGES OF INFECTED CASES WHICH SHOWED SOME REDUCTION AT FINAL READING  
(Number of Cases, 5)

CALYX				PELVIS				URETER			
RIGHT		LEFT		RIGHT		LEFT		RIGHT		LEFT	
NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%
4	80	2	40	4	80	1	20	2	40	0	00.0

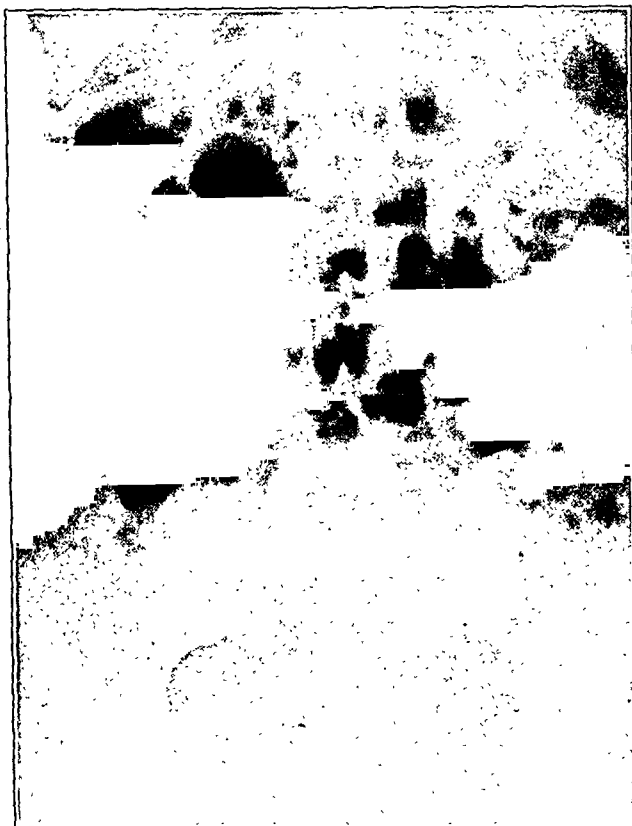


Fig. 5.—Four days postpartum, febrile. Compare size of left ureter and kidney pelvis with Figs. 3 and 4.

this group of infected patients. The contrast with Tables VI and VI-A is very striking.

#### DISCUSSION OF OBSERVATIONS ON INFECTED PATIENTS

We realize that this series of patients with puerperal infection is entirely too small to justify any conclusions, but the results are so outstanding that we feel inclined to postulate an hypothesis concerning the etiology of postpartum pyelitis.

It is well established that dilatation of the ureter is a primary factor in the production of pyelitis of pregnancy. Saitz<sup>12</sup> states that there must be a primary ureteral dilatation before pyelitis may develop; in-

fection is always secondary, and he says, "Repeatedly there may be dilatation with subsequent infection, but never infection without dilatation." Morris and Langlois,<sup>11</sup> Hofbauer,<sup>10</sup> Duncan and Seng,<sup>4</sup> and others, concur in this belief.

Why may not the same thing be true for pyelitis occurring during the puerperium? If intrauterine infection, even of a degree so mild as almost to escape recognition may cause dilatation of the ureter during the puerperium, it is reasonable to postulate that all patients so affected are possible candidates for postpartum pyelitis. In this small series of 5 patients with puerperal infection, the ureter remained dilated in 3, and redilated after a reduction in size in the other 2. It must be emphasized that none of this group with dilated ureters developed clinical symptoms of postpartum pyelitis, though 2 of the patients had transient costolumbar pain. Because of the findings in this group of 5 patients, we are tempted to believe that the primary factor in the production of a pyelitis, dilatation, is produced in some manner by an intrauterine infection developing during the puerperium.

Two cases of fatal puerperal infection seen in consultation during the past year are significant in this connection. In each instance the initial symptom was pain in the right flank which overshadowed the uterine findings. Despite the fact that the urine was practically negative, each patient was thought at the first visit to have postpartum pyelitis, and it was not until the other symptoms became more pronounced that the serious nature of the infection was discovered.

This conception of the etiology of postpartum pyelitis is purely an hypothesis suggested by the findings developing out of an investigation undertaken for the study of urinary tract involution in normal puerperal women. Because of the insufficient number of cases it is impossible to make any definite statement. The suggestions offered above partake of the nature of a preliminary report.

#### CONCLUSIONS

1. Each of the 41 patients showed some degree of dilatation of the right urinary tract prior to delivery, while the majority also showed dilatation on the left side.

2. More primiparas than multiparas had marked dilatation antepartum, and were more tardy in involuting postpartum.

3. A considerable decrease in urinary tract caliber was observed within twenty-four hours following delivery in 8 cases.

4. Of 12 normal patients, involution was complete in the majority by the ninth to the eleventh day.

5. The majority of 41 patients showed marked reduction in the caliber of the urinary tract by the end of the twelfth day postpartum.

6. Five patients having febrile puerperiums presented sluggish involution, and it is postulated that this delay may be the primary factor underlying the development of postpartum pyelitis.

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## ACUTE ANTERIOR (POLIOMYELITIS) COMPLICATING PREGNANCY\*

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ACUTE anterior poliomyelitis, apparently unknown as a definite disease entity prior to Underwood's<sup>1</sup> paper in 1784, has assumed a more and more prominent position in medicine during the past third of a century. Although much has been written concerning this disease, there are only a few scattered articles pertaining to the relationship of acute anterior poliomyelitis to pregnancy and to its occurrence during pregnancy. There are several possible explanations for the lack of literature dealing with the latter subject.

Acute anterior poliomyelitis is primarily a disease of childhood. In Vermont from 1912 to 1925 there were 848 cases of poliomyelitis, of which 176 or 23.5 per cent were over fifteen years of age. In Massachusetts from 1914 to 1923 there were 1594 cases reported, and only 145 or 9.09 per cent were over fifteen years of age. According to Wickman<sup>2</sup> and others the disease is slightly more common in males than females. Aycock<sup>3</sup> in a study of the age incidence of the disease concluded that "the majority of persons become immunized either subclinically or through unrecognized attacks of the disease" before they reach adult age.

Believing that an immunity to the virus of poliomyelitis in individuals who gave no history of having passed through an attack of the disease might be present, Aycock and Kramer<sup>4</sup> tested 75 normal individuals in Massachusetts and Vermont. Forty-six of the individuals were from urban communities and 29 were from rural districts. Of the urban population 69.6 per cent were immune by the neutralization test and only 20.7 per cent of the rural population were immune. In the age group fifteen to nineteen years, 85.7 per cent of the urban population and 50 per cent of the rural population were immune. In the adult group, 87.5 per cent of the urban and 40 per cent of the rural population were immune. The authors concluded that there is a wide spread immunity to poliomyelitis among individuals not known to have had the disease, and believe that this immunity originates in exposure to the virus, and from the extent to which it occurs and the order in which it develops that the virus spreads by person to person contact, the actual disease occurring in only a small portion of those exposed.

\*NOTE: For lack of space, the complete paper of Dr. McGoogan cannot be included in the Journal but may be had in the author's reprints.

That the immunity to poliomyelitis is equally extensive in warmer and cooler climates is shown in that the serum of 18 out of 21 normal adults in Georgia neutralized the virus.<sup>5</sup>

From these studies it must be concluded that the occurrence of the disease in women during pregnancy must be rare. If the rare occurrence is not recognized, or if recognized is not reported in the medical literature then the disease becomes, on paper, relatively more rare.

Alpers<sup>6</sup> in an extensive study of the cerebral and spinal complications occurring during pregnancy states that poliomyelitis complicating pregnancy is of rare occurrence.

Three cases of acute anterior poliomyelitis during pregnancy have been observed in Omaha, Nebraska, during the past five years. This led to a survey of the literature upon the subject and five similar cases were found.

The first case reported is that of Schell's<sup>7</sup> in 1906. Although he diagnosed the case as one of myelitis, a review of the history warrants the reclassification to that of acute anterior poliomyelitis.

Renault and Martingay<sup>8</sup> reported the second case in 1911.

Miller<sup>9</sup> in 1924 reported two more cases.

Foulkrod<sup>10</sup> in 1924 reported a case as probably poliomyelitis, but after a careful review of the case history, it should be classified as an acute infectious myelitis rather than a poliomyelitis.

Hornung and Creutzfeldt<sup>11, 12</sup> reported the fifth case in 1930.

The three cases occurring in Omaha follow, and the first two are from the private service of Charles W. Pollard.

CASE 1.—Mrs. J. The patient was a primipara aged twenty-four, who had her last menstrual period May 10, 1926. She was well except for mild morning nausea until August 23 when she developed rather severe nausea. The following day she felt faint and tired. On August 25 she developed tenderness in the back, pain on motion in the back and legs and was unable to stand. There was moderate vomiting and severe headache. These symptoms persisted for four days after which time the patient developed urinary retention and paralysis of the right leg. The urinary paralysis lasted only two days. The pain in the back and legs persisted for three weeks then began to abate and the paralysis began to improve. She was admitted to the Omaha Maternity on September 6, 1926, two weeks after onset of her disease, and an examination at that time revealed absence of the right abdominal reflex, weakness of the right leg and a bilateral Kernig sign. A lumbar puncture was done, the pressure being 4 mm. mercury. The protein content was 25 mg. per 2 c.c. of spinal fluid, and a cell count showed 14 cells per c. mm. A spinal fluid Wassermann was negative and a colloided gold curve was not remarkable.

The patient improved with massage to the right and left legs and after two months was walking without support. She went into labor on February 3, 1927, and after a normal labor delivered a male child weighing 6 pounds and 12 ounces. The placenta was expelled normally. The puerperium was normal. The child was apparently normal and is well at the present time. The patient has had one normal pregnancy since.

CASE 2.—Mrs. N. The patient was a para ii, aged thirty-two, who had her last menstrual period on May 14, 1930. She was well except for slight morning nausea and vomiting until August 24, 1930, when she developed a generalized muscle sore-

ness in back and legs as if she had influenza, and she became very drowsy. She felt well for the next two days when she had a recurrence of the symptoms. The following day she felt so ill that she was confined to her bed and developed chills, fever, and epigastric pain with nausea and vomiting. These symptoms continued for seventy-two hours. One week after the onset of her illness she developed shooting pains in both legs and back. The nausea, vomiting, and epigastric distress ceased and the temperature became normal. Toward evening of that day her left leg became so "tired" that she could not move it. The following morning she felt so well that she got out of bed and while making her toilet she collapsed and found that she could not arise. The following day she noticed that she could not arise from a sitting posture or sit down, but if she were helped up she could walk by holding onto a chair, pushing it before her.

She was admitted to the Bishop Clarkson Hospital on that day, and an examination by Dr. Robert Shrock showed weakness of the abdominal muscles, more on the left than on the right, bilateral weakness of the hip muscles, no complete paralysis of the legs although the thigh muscles were the weakest. Dr. Shrock concurred in the diagnosis of acute anterior poliomyelitis, involving the last four dorsal segments of the cord. The patient was treated by massage and exercise and after three months had returned to two-thirds of her normal muscular power of the muscle groups involved.

The pregnancy continued uneventfully until January 5, 1931, when the patient developed a rise in blood pressure to 140/90, with three-plus albuminuria and slight edema of the extremities and face. She was treated at the Omaha Maternity Hospital from January 18 to 22 for toxemia, and was greatly improved on her discharge. She had a return of symptoms however, and was readmitted to the Hospital February 6 with blood pressure 150/90, albuminuria 2-plus, slight edema of face and hands and slight headache. She again improved under toxemia treatment and on February 10 was awakened at 2 A. M. by mild lower abdominal pains. She delivered herself at 5:30 A.M. of a normal female child weighing 6 pounds. The placenta was expelled normally and there was little bleeding. The puerperium was uneventful. Six weeks following delivery the patient had recovered 90 per cent of the function and power of her involved muscles. The child was well and showed no deformities.

CASE 3.—This case is reported through the kindness of Dr. Frank J. Munk. The patient was a primipara, aged twenty-four, and in the third month of gestation. On April 28, 1926, she developed pains in lower abdomen, pain and soreness in the back, both legs, and the right arm. There was an associated intense headache, and the temperature was 102°. The patient became paralyzed in both legs and the right arm the day after onset and developed urinary retention and constipation. There was no impairment of sensation. A lumbar puncture showed a slight increase in pressure, but otherwise normal findings. On April 30, May 1, and May 2 the patient was given Rosenau's serum intraspinally. She required catheterization of the bladder during this time. The temperature gradually subsided and on May 7 was normal. At this time the patient began showing some recovery of motion in the right arm and return of bladder function, and of bowel function.

She was treated with massage and plaster splints to her legs with slight improvement.

On September 21, the patient went into normal labor, and delivered a premature (eight months) child, weighing 5 pounds. The child lived only two days, the cause of death is unknown but was thought to be prematurity. An autopsy was not done.

The mother has regained very little function of her lower extremities, and is able to get about only with the aid of supports. She has not been pregnant since.

The mode of infection in this case is interesting. Living in the patient's home was a graduate nurse who was nursing a case of acute poliomyelitis.



## EFFECT OF THE DISEASE UPON PREGNANCY

Any disease arising as a complication during pregnancy may affect the pregnancy. In the eight cases reported, the pregnancy itself was in no way affected. In the seven cases in which the disease occurred during the early months of gestation, there was no spontaneous interruption of the pregnancy nor was there intrauterine death of the child during the acute stage of the infection itself. What the ultimate effects in Miller's second case would have been are problematical, and undoubtedly Hornung's patient would have died undelivered had there not been the intervening cesarean section. One case (Munk's) delivered prematurely but five months after the onset and subsidence of the acute stage, and in view of the frequent occurrence of premature labor, it is doubtful if there was any relationship between the premature labor and the poliomyelitis. Although the series is small, it may be concluded that acute poliomyelitis occurring during pregnancy has no effect upon the pregnancy itself.

Pregnancy upon the other hand may be a factor in the severity and ultimate outcome of any disease already existing at the onset of gestation or occurring as an intercurrent infection. In only two cases out of the entire series, Miller's second case and Hornung's case, does pregnancy seem to have any deleterious effect upon the progress of the disease or its outcome. In Miller's second case, the patient was greatly improved following the interruption of the pregnancy. The patient had a paralysis of the bladder with a fulminating type of cystitis. The enlarged uterus evidently prevented a return of the normal tonus of the bladder, and a cystitis intervened as so frequently happens in those cases in which retention of urine, secondary to lesions in the spinal cord, occurs in paralytic bladders. Her long continued cystitis was undoubtedly the cause of her poor physical condition. Interruption of the pregnancy with resultant improvement of the patient's condition followed. In the remainder of the cases, although bladder paralysis was present, it was of short duration.

In Hornung's case the importance of the relationship of the extent of the paralysis to the duration of the pregnancy is clearly demonstrated. The patient developed an ascending paralysis involving the diaphragm with an increasing cyanosis. The aeration of the lungs in a normal pregnant woman at term is accomplished by a costal type of respiration rather than abdominal due to the restricted excursion of the diaphragm<sup>13</sup> and with emptying of the uterus, the chest is relieved. If the diaphragm becomes paralyzed then respiration is accomplished entirely by the accessory muscles. In an effort to obtain better aeration of the lungs already embarrassed by diaphragmatic paralysis, Hornung performed a cesarean section. The patient's condition appeared to have been temporarily improved as a result of this procedure in as much as she was not cyanotic. The disease was progressive and

the patient died. With an acute ascending paralysis in which there is involvement of the phrenic nerves, either partial or complete, it seems that emptying of the uterus should be done if the enlargement of the uterus is sufficient to encroach upon the diaphragm. This should be done not so much as an effort to check the progress of the disease but to improve the patient's lung aeration and postpone the onset of fatal respiratory paralysis. This procedure coupled with the use of a Drinker respirator<sup>14</sup> might give a favorable outcome to an otherwise hopeless case.

Cesarean section in this type of case might be considered as being entirely too radical a procedure. Another possible line of treatment that might be suggested would be the use of the Drinker apparatus combined with general supportive measures. If these failed then a postmortem cesarean section should be considered.

\* \* \* \*

That pregnancy may have some effect upon the rapidity of the process of recovery is possible but is not conclusively demonstrated in the cases reported.

In Case 2 of the Omaha series the improvement was slightly more rapid following delivery. In Case 3 there was no further improvement following delivery, and a similar condition occurred in Miller's first case. It is possible therefore to suggest that in the first instance the added strain of pregnancy retarded complete recovery before term, but after delivery, the load being removed, the regeneration progressed more rapidly. In the other instances no improvement followed delivery but perhaps the disease would not have been as extensive if pregnancy had not been present.

Fernandez<sup>21</sup> cites the case of a patient who became pregnant two months after the onset of her disease, and whose improvement following delivery by cesarean section at term was quite marked.

From the history of these cases there comes a suggestion that possibly pregnancy has some influence upon the rapidity of recovery from the effects of the poliomyelitis.

#### EFFECT OF THE DISEASE UPON THE CHILD

The transmission of disease from mother to child in utero can occur. Of the diseases involving the central nervous system, it has been shown that epidemic encephalitis sometimes may infect a fetus if the mother has the disease (Mercier<sup>25</sup>), (Marinesco<sup>26</sup>), (Jorge<sup>27</sup>), (Levaditi<sup>28</sup>), and that encephalitis in utero may be acquired from other causes (Paterson and Carmichael<sup>29</sup> and Virchow<sup>30</sup>). Kramer and Wright<sup>31</sup> reported the case of a woman with cerebrospinal meningitis who died before delivery but the autopsy revealed a similar condition in the child. Acute anterior poliomyelitis is an acute infectious disease, and the possibility of fetal involvement becomes apparent. By what route the virus reaches the

nervous system from the nasopharynx has not been definitely determined. The two possible routes are, (1) via blood stream, and (2) via the perineural lymph spaces of the olfactory nerve. Experimental demonstrations have supported the latter route (Draper<sup>32</sup>). If the latter route is the only route and the virus does not enter the blood stream, then it seems as if it would be anatomically impossible for the fetus in utero to develop acute anterior poliomyelitis.

The virus has not been found at any stage of the infection in the blood in human beings, though in the monkey, on the first day of symptoms it has been detected in one instance when large amounts of the virus were inoculated.<sup>33</sup> After intravenous injection of the virus into the blood, the virus tends to disappear so that after one hundred and twenty hours it is no longer present.<sup>34</sup> The finding of the virus in the lymph glands (Amoss<sup>35</sup>), (Levaditi<sup>36</sup>), supports the theory that the virus must be blood borne at some stage of the disease, possibly very early and its presence of very short duration. If the virus is blood borne at some stage of the infection before it localizes in the central nervous system, then it seems possible that it might be transmitted via placenta to a fetus in utero.

In only one of the eight cases reported is there any suggestion of intrauterine poliomyelitis and that is in Miller's first case in which the child was born with a bilateral club foot. Miller, however, points out that in view of the frequent occurrence of this deformity, it cannot be concluded that it is the result of a transmitted intrauterine poliomyelitis. One infant, delivered before the period of viability, was in no way deformed; and one was premature and died in forty-eight hours, yet it showed no external evidence of deformity. The other five children were perfectly formed.

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#### EFFECT OF THE DISEASE UPON LABOR

The effect of the paralysis and bony deformities subsequent to an attack of poliomyelitis upon labor depends upon a number of factors, (1) the extent of the paralysis, (2) the size and shape of the pelvis, (3) the size of the child and the relationship of the size of the head and the pelvis to one another, and (4) the general condition of the mother.

\* \* \* \*

Miller<sup>9</sup> discussed the possibility of prolonged bladder paralysis interfering with the second and third stages of labor. A full bladder might interfere with the normal contractions of the third stage and increase the possibility of a postpartum hemorrhage.

That the onset of uterine contractions occurs in spite of spinal cord lesions has been shown by many experiments and clinical cases. Normal delivery can and will occur with all the nerves to the uterus severed.

That the third stage may also be without incident is shown by Good's experiments.<sup>53</sup> He performed transection of the cord upon a pregnant guinea pig twenty-four hours before a cesarean section was done. Following the cesarean section the uterus contracted promptly without hemorrhage, and he concluded that the sympathetic nervous system and not the spinal cord controlled uterine contractions. Rudolph and Ivy<sup>65</sup> studied the uterine contractions in the postpartum uterus of the dog and came to the conclusion that there is an extrinsic and intrinsic mechanism, one resident in the uterine wall and the other in the uterovaginal ganglia, the former being the most important.

Very little difficulty should be expected with delivery in any of its stages, unless there is disproportion or malposition present, in a woman who has had poliomyelitis either preceding or during pregnancy. The six patients, who delivered via naturalis in the above reported series in which poliomyelitis occurred during pregnancy, delivered without difficulty, labor was not unduly prolonged, and the third stage was normal as to time and blood loss.

#### DIAGNOSIS OF ACUTE ANTERIOR POLIOMYELITIS

Luther and Aycock<sup>66</sup> in 1929 studied a large series of cases in order to determine the incubation period of the disease and from their studies concluded that the apparent incubation period falls within a period of from six to twenty days. They found evidence that "the infectious period of the disease may extend from the fourteenth day preceding the onset of symptoms to at least the fifth day of the disease."

Luther and Aycock<sup>67, 68, 69</sup> have given methods of making the diagnosis in the preparalytic stage. The patient is taken ill with fever, headache, and occasional gastrointestinal disturbances, nausea, vomiting, and constipation. Drowsiness and a desire to be let alone are frequently observed. These findings resemble most any acute infection and one should be on the watch for the following symptoms: flushed face, a rapid pulse, more prostration than the temperature warrants, and evidence of meningeal irritation, such as a coarse tremor, slight rigidity of the neck, stiffness of the spine, a very slight Kernig's, but with hyperactivity of the deep reflexes which later diminishes. A lumbar puncture with spinal fluid examination reveals the fluid to be under slightly increased pressure, an increase of white cells usually 50 to 250 per c.mm., increase of globulin and normal sugar, and the colloidal gold curve shows an early slight rise.<sup>70</sup> The patient may or may not develop a flaccid paralysis within the next forty-eight to seventy-two hours.

#### DIFFERENTIAL DIAGNOSIS OF ACUTE ANTERIOR POLIOMYELITIS

Acute anterior poliomyelitis may be confused with several other diseases which run a similar course or which show weakness or paralysis simulating that which occurs in poliomyelitis. A careful history and physical examination with study of the reflexes and sensory changes, accompanied by spinal fluid studies, will aid in making the correct diagnosis. Many of the acute infections in their early stages simulate the

early stage of poliomyelitis before the onset of the paralysis. One of the common diseases so confused in influenza, which the patient, reported as Case 2 of the Omaha series, thought she had before the onset of her paralysis. Renault and Martingay's patient had a similar condition. Acute articular rheumatism and typhoid fever are also commonly confused with poliomyelitis. Epidemic encephalitis with its prodromal symptoms of fatigue, headache and myalgia may so closely resemble poliomyelitis as to make the differential diagnosis difficult. However, encephalitis is primarily a disease of the higher nervous centers, and poliomyelitis a disease of the spinal cord. The presence of an epidemic aids in making the diagnosis.

Epidemic cerebrospinal meningitis may be confused with the encephalitic form of poliomyelitis as the symptoms of headache, vomiting, lassitude, fever and rigidity of the neck usher in both diseases. Spinal puncture and the finding of the meningococcus makes the diagnosis. The paralyzes are different, as that of poliomyelitis is flaccid and of meningitis spastic.

An important differential lies between acute anterior poliomyelitis and the neuritides, the mononeuritis and the polyneuritis. In mononeuritis any nerve may be involved. Fink<sup>71</sup> reports a series of cases in which the nerves of the shoulder girdle, the facial nerve, the ulnar nerve, the median nerve, and the lumbar nerves respectively were the site of the disturbance.

\* \* \* \*

#### TREATMENT

Treatment of acute anterior poliomyelitis should be directed toward lessening the damage to the central nervous system. Early diagnosis and institution of therapy early are of great importance. The general opinion is that the use of human convalescent serum seems the most rational form of treatment, following the technic of Aycock, Luther, and Kramer.<sup>81</sup>

Rosenau had used antistreptococcic horse serum in 1,300 cases and reports favorable results. The best results are obtained with serum therapy in the preparalytic stage but it may be used with less favorable results in the early paralytic stage. After the paralysis appears, the diagnosis becomes quite apparent, and treatment should be directed toward the prevention of deformities and increasing the patient's general condition. MacAusland describes in great detail the treatment of this phase of the disease and what methods should be used to prevent the development of deformities.

The presence of a pregnancy, after reviewing the series of cases presented, in no way should alter the accepted forms of treatment for poliomyelitis. In the majority of cases when the disease occurs early during the gestation period, the pregnancy can be disregarded. If it

occurs late as in Hornung's case, or causes a cystitis as in Miller's case then interruption of pregnancy should be considered. Pregnancy following a recent poliomyelitis should be advised against, because of the possibility of the pregnancy affecting the rapidity of recovery as is suggested in Fernandez's case.

#### SUMMARY

1. Eight cases of acute anterior poliomyelitis complicating pregnancy are referred to, five from the literature and three additional cases.

2. Acute anterior poliomyelitis complicating pregnancy has no effect upon the pregnancy itself.

3. Pregnancy may have some effect upon the rapidity of the patient's recovery from the disease. It may increase the severity of the poliomyelitis, or its complications, such as, cystitis, and diaphragmatic paralysis.

4. Interruption of pregnancy should not be done except in those instances in which the uterus encroaches upon the diaphragm and there is diaphragmatic paralysis; or in the case of a severe cystitis, or other complications.

5. Intrauterine poliomyelitis if it does occur must be very rare.

6. Passive transmission of maternal immunity to the child does occur.

7. Very little difficulty should be expected with delivery in any of its stages, unless there is malposition or disproportion present in a woman who has had poliomyelitis either preceding or during her pregnancy.

8. Pregnancy following a recent poliomyelitis should be advised against.

Although eight cases is a small series from which to draw conclusions, much of interest has been learned from them. As more cases are reported, and there undoubtedly will be as the disease is apparently becoming more common, a better understanding of the pathology of acute anterior poliomyelitis and pregnancy will be reached.

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420 SOUTH TWENTY-FIFTH AVENUE.

**Villarama and Galang: Typhoid Fever in Pregnancy.** J. Philippine Islands Med. Assn. 10: 311, 1930.

Sixty-four patients, consisting of pregnant and puerperal women affected with typhoid fever, formed the subject of these studies. Typhoid fever terminated pregnancy in about 78 per cent of the cases, but the termination of pregnancy did not in any way cut short the course of the disease.

Fetal mortality amounted to 60 per cent of the fetuses born. Maternal mortality was about 26 per cent, more deaths having occurred among patients affected during puerperium than among those affected during pregnancy.

Of the three cases with positive blood culture for *Bacillus typhosus* 2 recovered and 1 died. All the patients who had previously been inoculated with antityphoid vaccine recovered.

C. O. MALAND.

# RADIUM THERAPY IN UTERINE HEMORRHAGES OF BENIGN ORIGIN\*

## A CLINICAL STUDY OF 105 CONSECUTIVE CASES

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WHEN radium was first introduced as a therapeutic agent in gynecology it was employed entirely for the treatment of malignant neoplasms of the uterus, and it found its greatest field of usefulness in cancer of the uterine cervix. As this powerful agent became better understood, its curative properties were applied likewise to noncancerous or benign lesions of the uterus.

Radium therapy offers two important advantages: the first, the absence of primary mortality in properly selected cases and the second, the short period of hospitalization which its employment necessitates. The largest number of patients who need radiation for uterine hemorrhages are married women in middle life, nearing or at the menopause, who are very much needed at home because of growing children and the saving of time is an important consideration. We are all familiar with the severe uterine hemorrhages at the menopause, without gross macroscopic changes in the uterus and adnexa. Before the advent of radium, several curettages having failed, hysterectomy was resorted to. One, and sometimes two blood transfusions had to be administered to women so afflicted in order to get them in condition to stand an operation as extensive as the ablation of the uterus. Again, there were the worries of the first few postoperative days in many of these patients who, because of secondary anemia, were considered poor surgical risks. The period of convalescence following such an intervention was rarely less than four weeks. While many operators have been able to report series of one hundred or more hysterectomies without a fatality, it is an admitted fact that the mortality of this operation, in the hands of well trained surgeons, varies between 2 and 3 per cent for the subtotal and slightly higher for the total removal of the uterus. It is, of course, much higher in the hands of the occasional operator. Radium used for the same conditions should have no primary mortality, when properly employed, and if it does, it is strikingly less than that of hysterectomy. The period of hospitalization, about three days, in the case of radium, against an average of two weeks in the case of hysterectomy, is greatly in favor of the former.

In all benign lesions of the uterus, where the application of radium may be indicated, the principal symptom is hemorrhage. Radium, there-

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fore, is of greatest value in small fibromyomas and in menorrhagia and metrorrhagia in uteri presenting no gross macroscopic lesions. Hypertrophy and hyperplasia of the endometrium fall into this group. Again, the patients having uterine hemorrhages may be placed in three classes according to their ages, (1) the hemorrhages of adolescence and of young women; (2) the hemorrhages of middle life, and (3) the hemorrhages of the menopause and those occurring after the menopause.

THE MAIN CONTRAINDICATIONS TO RADIUM THERAPY ARE LARGE FIBROMYOMAS, INFLAMMATION OF THE ADNEXA AND OVARIAN TUMORS

Insofar as fibromyomas are concerned, radium may be used as a curative agent in the smaller tumors or it may be used as a prophylactic

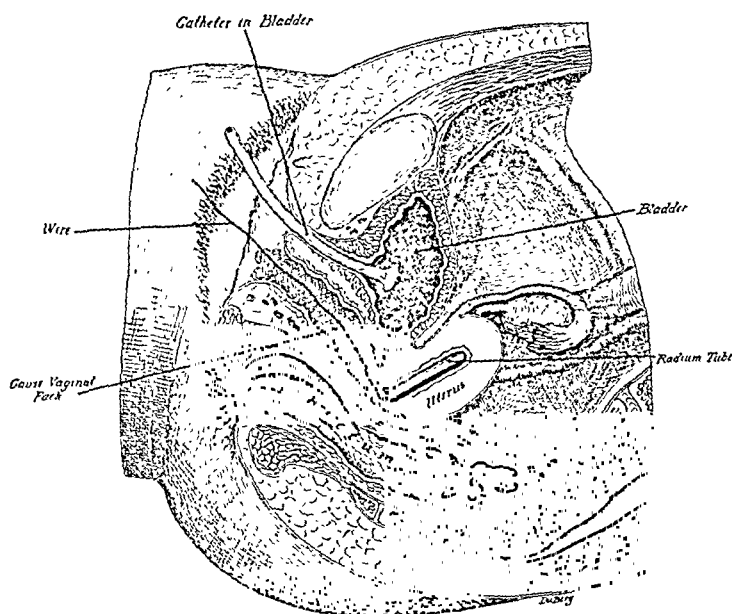


Fig. 1.—Sagittal section of the pelvis showing the radium tube in the uterus, the vaginal gauze pack, and the self-retaining catheter in the bladder.

agent to arrest hemorrhage from the larger tumors, thus permitting the patient to improve in general health and allowing the performance of a hysterectomy under safe conditions at a later date. Subserous fibromyomas, if pedunculated, are but little affected by radium. Moreover, radium causes necrosis and sloughing, thereby increasing the amount of bleeding in the submucous variety. The best results are obtained in the intramural or interstitial tumors. The age of the patient plays an important rôle in the treatment of these new growths. In young women myomectomy and conservation of the functions of menstruation and reproduction should be resorted to when possible. A fundic hysterectomy, saving enough endometrium to allow menstruation when it is impossible to save the function of reproduction, should be the next step in order. A subtotal hysterectomy, in the presence of a healthy cervix and a total hysterectomy when this organ is irritated or severely lacerated, together

with the conservation of one or both adnexa, should be performed when the tumors are voluminous or too numerous to allow the application of the first two mentioned procedures. After the menopause both tubes and ovaries should be removed with the uterus. In the younger women radium is employed only when there are definite constitutional contraindications to an operation. At the menopause radium may be chosen for the small tumors, those not exceeding a three-month pregnancy in size and for the poor surgical risks, while surgery may be selected when the opposite is true.

The successful use of radium in the treatment of benign lesions of the uterus rests upon the ability to perform a satisfactory bimanual examination to rule out adnexal infection and inflammation, together with ovarian neoplasms.

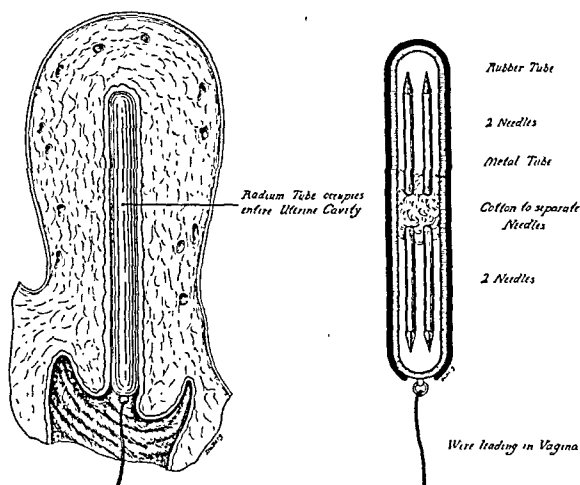


Fig. 2

Fig. 3

Fig. 2.—The radium tube usually occupies the entire uterine cavity except in the case of fibromyomas, where it is placed as near the fundus as possible.

Fig. 3.—The radium applicator (diagrammatic). Four radium needles 0.0125 gm. each, are used, making a total of 0.050 gm. The filtration is through one millimeter of brass and one-half a millimeter of rubber, filtering the alpha and beta rays and delivering the gamma rays.

An examination of my personal records from September 27, 1927 to August 10, 1931 shows that I have treated 105 consecutive cases of uterine hemorrhage of benign origin with radium during this period of time.

These 105 cases are classified as follows:

Fibromyomas	15
Uterine hemorrhages of adolescence and of young women	7
Uterine hemorrhages of middle life	72
Uterine hemorrhages after the menopause	11
	<hr/>
	105 Cases

#### TECHNIC OF APPLICATION

A laxative is given the day before and a soapsuds enema the evening previous to operation. The vulva and vagina are scrubbed with liquid green soap and irrigated with a solution of potassium mercuric iodide 1-1000. One of the methods of dry

preparation may be used if preferred. The cervix is exposed, its anterior lip grasped with a suitable vulsellum and in the presence of a cervical discharge, the cervical canal is swabbed with tincture of iodine 3½ per cent, applied on a cotton wound applicator. The cervix is gently dilated and the uterine cavity curetted. A diagnostic curettage, with histologic examination of the curettings, is performed in all cases to rule out malignancy. The radium applicator consists of a brass tube 5 cm. in length and 1 mm. in thickness, into which is disposed 50 mg. (0.050 gm.) of radium in the form of radium sulphate. The brass tube, at the end of which a fine nonrusting wire is attached, is covered by a thin rubber sac 0.5 mm. thick. The tube is placed in the uterine cavity and usually occupies its whole length except in the case of fibromyomas. This apparatus filters out the alpha and the beta rays and allows gamma radiation. The vagina is firmly packed with plain sterile gauze; medicated gauze, such as iodoform and xeroform, is never used in order to avoid secondary radiation. A self-retaining catheter is introduced in the bladder and the patient is returned to bed. During the period of radiation she stays quiet in bed, in dorsal decubitus, to prevent disturbing the apparatus. The radium is left in for a definite number of hours according to the dose which is necessary; thus, if the radium is left in thirty-six hours the dose would be 1800 mg. hours. She is placed on a liquid diet, including milk and morphine sulphate or pantopon, in appropriate doses, are prescribed when necessary for pain and insomnia. The patient may be allowed out of bed the day the radium is removed or the next day if she prefers. During the period of radiation there may be a certain amount of nausea; rarely is emesis present. Occasionally, there may be abdominal cramps caused by the presence of the radioactive tube. The smaller the tube used, the less likely is the presence of pain. These symptoms are generally over after the first twenty-four hours if the radium is left in for a longer period of time. If the radium is introduced shortly after a period the following menstruation may be missed. On the other hand, if it is applied just before an expected catamenia this may occur as a regular period. I have not seen more than two menstruations when a sterilizing dose was employed, except in one instance. The high temperature reactions spoken of by some authors have not been met in this series of cases. The highest thermic reaction encountered was 101° F. (38.3° C.). For about two months, rarely more, there is a moderate leucorrhea which is easily controlled by a daily douche. A satisfactory one is obtained by dissolving two teaspoonfuls of "antiseptic powder" (National Formulary) in two quarts of warm water.

When a sufficient dose of radium has been employed the symptoms of the menopause soon follow. These, as a rule, are not more severe than those of the physiologic menopause.

#### ANESTHESIA

In the series of 105 cases reported, local infiltration anesthesia was used 9 times, spinal anesthesia 4 times and nitrous oxide, oxygen, ether anesthesia 92 times. Local infiltration anesthesia gives such satisfactory results in this type of case that I feel it will largely replace the other two forms in my future cases. Its administration is simple, and it is the safest procedure to use, especially in women who have lost a great deal of blood. A one per cent solution of novocaine is employed. With a long, thin, flexible needle 5 c.c. are injected at the base of each broad ligament to block the sympathetic plexuses of Frankenhäuser, 5 c.c. are placed anteriorly at the level of the bladder reflection and the same amount posteriorly. After a few minutes, the cervix is insensitive and the dilatation may be begun. For spinal anesthesia, in these cases, I

have never used more than 100 mg. of sterile novocaine crystals. These are dissolved in 2 c.c. of spinal fluid and slowly reinjected.

#### STATISTICS

##### Fibromyomas Uteri, 15 cases.

The ages of the fifteen patients with fibromyoma uteri in this group were as follows: Thirty-six years; thirty-seven years, 3 patients; thirty-nine years, 2 patients; forty years; forty-one years; forty-two years, 2 patients; forty-four years; forty-seven years; forty-eight years; forty-nine years and fifty-three years.

In all cases the myomas were small. In eleven women a dose of 1800 mg. hours was administered; in two others a dose of 2400 mg. hours was given. In the case of a woman, thirty-six years old, who had a myoma the size of an orange, about 7.5 cm. in circumference, at the right uterine horn and who also had a mitral stenosis and regurgitation, a radium dose of 1400 mg. hours was used on December 2, 1926. This completely arrested the bleeding until December, 1927, when it recurred. Examination, then, revealed a myoma in the same region. A second dose of radium, consisting of 1800 mg. hours, was given, making the total dose 3200 mg. hours. This stopped the bleeding permanently and caused the tumor to disappear. A woman, forty-one years of age, having multiple small fibromyomas, was given 1400 mg. hours and subsequently 1800 mg. hours, making a total dose of 3200 mg. hours. This brought on permanent amenorrhea, but a hysterectomy, with the ablation of the adnexa, was later performed because of pelvic pain. The details of her case follow:

Mrs. — Case No. 4947, aged forty-one, consulted me on November 4, 1927. She complained of menorrhagia and metrorrhagia, the periods lasting nine days with an interval of two weeks. She had been married fourteen years; she had two miscarriages between three and four months of pregnancy and one child at term, delivered instrumentally, who subsequently died.

The physical examination, except for secondary anemia and a few nabothian cysts of the cervix, was negative. A diagnostic curettage was performed on November 9, 1927. The histologic diagnosis was hyperplasia of the uterine mucosa. At this time radium was applied to the uterus, a dose of 1400 mg. hours being given. Following the radium application the patient started to flow on December 13, 1927 and flowed freely for five days, after which amenorrhea occurred until August 22, 1928 when the flow recurred and she began to pass large clots of blood. Drug therapy had no effect on this flowing. On October 13, 1928 a second dose of radium, consisting of 1800 mg. hours, was given, making the total dosage 3200 mg. hours. This brought on a permanent amenorrhea. The blood improved considerably so that it was within normal limits at this time. The patient, however, was complaining of pelvic pain, especially on the left. This pain was not relieved by local treatments. Her condition had so improved since her first visit that it was decided to do a hysterectomy in order to relieve her of the pain she constantly complained of.

On January 7, 1929 a blood transfusion, consisting of 600 c.c. of citrated blood, was administered. On January 8, 1929 a supravaginal hysterectomy, with coning of the cervix and removal of the adnexa, was performed. The convalescence was uneventful. The pathologic report was: "Multiple uterine myomas, hyperplasia of

the uterine mucosa, chronic cervicitis, localized fibrosis of the uterus, sclerotic ovaries." The fibroids were diffuse in the uterine wall and had not been felt on bimanual examination. The patient was discharged from the hospital in excellent condition and has remained well since.

In all fifteen cases a diagnostic curettage was performed prior to the radium application. Histologic examination of the curettings ruled out malignancy in all of them. In one of these women three large hemorroidal masses were removed under local anesthesia in addition to the radium application. In one other, whose blood examination showed severe secondary anemia, a transfusion of 600 c.c. of citrated blood was administered before the insertion of radium.

*Uterine Hemorrhages of Adolescence and of Young Women, 7 Cases.*—There were seven cases in this group. The ages were sixteen years in two, eighteen years in one, nineteen years in two, and twenty-four years in two. The complaint was menorrhagia in five and menorrhagia and metrorrhagia in the other two patients. The radium dosage was 400 mg. hours in two patients, in one of them a second dose of 500 mg. hours was given three months later, 500 mg. hours in two and 600 mg. hours in three.

Hemorrhage was arrested and regular periods established in five of these patients. In one of them a second dose of radium had to be given three months later, after which the excessive flowing at the periods ceased. In the case of a young woman, twenty-four years of age, a radium dose of 600 mg. hours had been successful in temporarily arresting the bleeding, but she is now flowing more than the normal at her periods. A second small dose of radium has been advised, but not given as yet. In the case of a single girl, nineteen years old, a 600 mg. hour dose had but little effect on the bleeding. A second dose was advised; this advice was not taken, however, and a hysterectomy was performed by another surgeon.

In all these cases medical and endocrine treatment had been tried without result before resorting to the use of radium.

#### UTERINE HEMORRHAGES OF MIDDLE LIFE, HYPERTROPHY AND HYPERPLASIA OF THE ENDOMETRIUM, 72 CASES

##### *Ages*

Between 29 and 35 years.....	6
Between 35 and 40 years.....	12
Between 40 and 45 years.....	24
Between 45 and 50 years.....	25
Between 50 and 55 years.....	5

##### *Radium Dose*

500 mg. hrs.....	1	1650 mg. hrs.....	1
1200 mg. hrs.....	6	1700 mg. hrs.....	2
1250 mg. hrs.....	1	1725 mg. hrs.....	2
1400 mg. hrs.....	3	1800 mg. hrs.....	50
1450 mg. hrs.....	1	2250 mg. hrs.....	1
1500 mg. hrs.....	1	2400 mg. hrs.....	3

*Additional Operations in This Group*

Bilateral trachelorrhaphy	5
Amputation of cervix	11
Biopsy of cervix	2
Cervical polypectomy	2
Puncture of nabothian cysts	1
Anterior colporrhaphy	2
Colpoperineorrhaphy	17
High vaginal fixation of uterus	1
Kelly operation for relaxed vesical sphincter	1
Reconstruction of right labium minus	1
Hemorrhoidectomy	1

In all seventy-two cases a diagnostic curettage was performed.

In the case of a woman fifty years old the following pathologic report was received: "Chronic inflammation with hypertrophied endometrium, epithelial cells atypical. The patient should be watched carefully." A radium dose of 1800 mg. hours was given on February 25, 1928. She has been well since.

## UTERINE HEMORRHAGES AFTER THE MENOPAUSE, 11 CASES

AGE	DIAGNOSIS	RADIUM DOSE
52	Hypertension. Hyperplasia of endometrium. Previous amputation of cervix	1200 mg. hrs.
57	Hyperplasia of endometrium. Cervical polyp	1800 mg. hrs.
66	Hyperplasia of endometrium. Cervical polyp	1800 mg. hrs.
59	Hyperplasia of endometrium	1800 mg. hrs.
63	Hyperplasia of endometrium. Nabothian cysts	1200 mg. hrs.
60	Hyperplasia of endometrium. Previous interposition of uterus	1200 mg. hrs.
60	Atrophied uterus	1200 mg. hrs.
62	Atrophied uterus	1800 mg. hrs.
63	Atrophied uterus	1800 mg. hrs.
63	Atrophied uterus	1750 mg. hrs.
70	Ulceration of vaginal vault. Histologic examination showed no malignancy. Radium pack	600 mg. hrs.

One patient in the series had a hysterectomy at a later date because of recurrent hemorrhages following a radium dose of 1725 mg. hours. The bleeding had been temporarily arrested so that the operation could be performed safely because of her improved general condition. The history of her case follows:

Mrs. — Case No. 4304, aged forty, was seen in consultation on March 3, 1927. She complained of flowing daily, although scantily, for a month and a half and of having a stain of blood following coitus. She had been married ten years; she had five children, one of whom had been delivered by vaginal cesarean section for eclampsia. On March 5, 1927 a trachelorrhaphy had been performed to repair old lacerations. On March 12, 1928 she had a dilatation and curettage and suture of the anterior lip of the cervix which had again become lacerated following delivery. The pathologic report showed chronic hyperplastic endometritis and polypoid hyperplasia. She was again seen on April 22, 1929; she had severe menorrhagia and secondary anemia, her hemoglobin being 50 per cent. On May 1, 1929 the bleeding had stopped and her condition was somewhat better. Under local anesthesia radium was introduced in the uterus and a dose of 1725 mg. hours administered. She reported

on February 18, 1930 and stated that she had started to flow again in December, 1929. She had then been bleeding for a month and had pain in the region of the left adnexa. She was sent to the hospital and on March 26, 1930 a supravaginal hysterectomy, double salpingo-oophorectomy, and appendectomy were performed. She was discharged well from the hospital. The pathologic report was as follows: "Microscopic examination of sections of the uterus show atrophic and essentially negative mucosa. The wall of the uterus is essentially negative except for hyalin thickening of the vessel walls, probably the result of involution changes. Sections of the ovary show many old corpus luteum scars and no evidence of active ovulation. Sections of the tubes show atrophy of the epithelium and simplification of the mucosal folds." On May 23, 1930 she reported for examination at which time it was found that the incision was well healed; the cervix was healed and well suspended and all vaults were clear. She was feeling well and has remained so.

In all cases, except in the case of the woman with ulceration of the vaginal vault, a diagnostic curettage was performed and the curettings examined histologically. In the four atrophied uteri but little endometrium was obtained. However, the radium stopped the bleeding in these four patients. The cervical polyps were resected and the nabothian cysts fulgurated. The ulcer of the vagina healed and the hemorrhage stopped in the six women with hyperplasia of the endometrium.

#### SUMMARY

One hundred and five women were treated with radium for uterine hemorrhages of benign origin. There was no mortality following this form of treatment in this series. Fifteen women having small fibromyomas, smaller than a two months' pregnancy, were treated. In 14 of them the tumors disappeared and permanent amenorrhea was established; in the fifteenth, although menstruation had completely stopped, a hysterectomy was performed at a later date for pelvic pain. In 7 cases of uterine hemorrhages of adolescence and of young women, where the smallest dose was 400 mg. hours and the largest dose 600 mg. hours, 4 were benefited with one dose, one was improved after a second dose, one needs another small dose, and the last had a hysterectomy performed by another surgeon when menorrhagia returned after a 600 mg. hour dose. In the group of uterine hemorrhages of middle life comprising 72 patients, one woman who had a dose of 500 mg. hours was improved and her menstruation continued. In 72 who had sterilizing doses 70 had permanent amenorrhea and were considered cured. In one of them hysterectomy was resorted to sometime after a 1725 mg. hour dose, for the return of the hemorrhages. Her physical condition had so improved during the period of amenorrhea produced by the radium, that the reaction from operation was slight and she made an uneventful recovery. I am sure the result would have been different had hysterectomy been attempted at the time she was subjected to radiation. In addition to the radiation there were 11 distinct types of operation performed on 44 women in this group. The 11 women having hemorrhages after the menopause saw cessation of the bleeding and were permanently improved. No pregnancies occurred in any of the women after radiation.

## CONCLUSIONS

1. Radium employed in suitable doses, in properly selected cases, is a valuable agent in the treatment of uterine hemorrhages of benign origin.

2. It finds its greatest field of usefulness in women near or at the menopause, having severe hemorrhages from uteri showing no gross macroscopic lesions, as in hypertrophy and hyperplasia of the endometrium.

3. It should be used cautiously, to avoid hysterectomy, in the hemorrhages of adolescence, and only after medical, endocrinal and hemostatic treatment have failed. Here minute doses should be employed. I have never gone above 600 mg. hours in this type of case.

4. It should not be used to regulate the menstrual periods and in an attempt to favor pregnancy, because of the risk incurred by the product of conception.

5. It is of value in treating small fibromyomas of the interstitial type, especially in women nearing the menopause.

6. A single application, giving an appropriate dose, is sufficient to bring on permanent amenorrhea.

7. These cases may be successfully treated with a small amount of radium (0.050 gm.), and with a minimum amount of apparatus.

270 COMMONWEALTH AVENUE.

(For discussion, see page 283.)

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## THE TOXEMIAS OF PREGNANCY WITH SPECIAL REFERENCE TO LIVER FUNCTION

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### INTRODUCTION

THERE is no difficulty in making a differential diagnosis between a typical nephritic toxemia of pregnancy and eclampsia. Between these two extremes is a large number of cases not so amenable to classification. It is necessary only to note the many classifications which exist to realize how little is known of toxemias of pregnancy.

Only occasionally eclampsia is not recognized. Pregnancy complicated by nephritis is usually diagnosed. The vomiting toxemias are relatively easily differentiated. Beyond these types little is definitely known. The large number showing, early or late in pregnancy, hypertension, albuminuria, and various toxic symptoms, some of them eventually developing eclampsia, some responding to treatment, and some presenting evidence of lasting renal damage, comprise the greatest number and are by far the most confusing to classify.

The present study was undertaken hoping that a detailed and correlated clinical and biochemical study of a group of pregnancy toxemias



and control cases might help in this classification. More than any other phase of the work liver function was stressed. Especially was it desired to formulate some prognostic index, some means of determining the final outcome of patients when first they became toxic. The value of such a procedure, if it were possible to elaborate one, would be unequivocal.

A series of toxemias contrasted against a series of controls is here presented. The history of each patient was carefully taken, with especial reference to previous obstetric toxemia or entities which might predispose to toxemia. Physical examination including ophthalmologic examination by a competent eye man was done. Detailed facts regarding the labor, the baby and infarction of the placenta were noted. The post-partum period was observed in most cases for from one to six months. The laboratory work comprised frequent readings of the blood pressure by the same observer, and analyses of the blood and urine. Renal function tests were made according to the method of Mosenthal. Liver function was studied by means of the nitrogen partition in the blood, the icterus index, and van den Bergh tests, and by quantitative determinations of the urobilin in blood and urine. As particular importance has been given to the urobilin findings in this paper, the technic of its detection as well as a short summary of previous pertinent investigations with this substance will now be discussed.

*Urobilin.*—Urobilin is formed from the bile pigment bilirubin. It is believed that bilirubin is reduced by bacteria in the intestine to urobilinogen which is reabsorbed by the blood stream and there oxidized into urobilin. It reacts with a characteristic fluorescence to certain acetate compounds, a fact Elman and McMaster have utilized for a quantitative test which has been employed in this study.

In normal urine there is found not more than 3 mg. of urobilin per 100 c.c. of urine. This concentration is not usually exceeded in the urine of normal pregnancy. Urobilinuria, however, occurs in many pathologic conditions. To conclude that its presence indicated primary liver damage would not be accurate. For example, organic heart disease may give rise to urobilinuria. Edelman shows that the degree of cardiac decompensation may be measured by the quantity of urobilin found in the urine. In this series 3 out of 5 syphilitic patients had excessive urobilinuria, but in only 1 of these was toxemia present, the other 4 being controls. Any disease which breaks down the red blood corpuscles may cause the appearance of this pigment in the urine. It is believed, however, that liver damage and consequent dysfunction causes the urobilinuria. Finally, it has been shown by Warthin that the urobilin content of the urine varies greatly within twenty-four hours, so that analysis of the total daily output is advisable.

Much work has been done with urobilin in pregnancy. Walthard believes that it is found in normal pregnancy. Litzenberg found it in the urine of 25 per cent of pregnant women in a series of 200 cases, while it was absent in 71 nonpregnant

controls. He uses the phrase "liver of pregnancy." King tried to differentiate nephritic and hepatic toxemia by means of the presence or absence of urobilinuria, but was unsuccessful. Barnard studied the urine of 115 pregnant women. About 80 per cent showed urobilinuria at one time or another. She included no details, but speaks of these women as being apparently normal. Berkeley depended upon increased urobilinuria as a criterion for induction, and felt that was the best and perhaps the only safe test upon which to interrupt pregnancy for toxemia.

Some of this work presents evidence that urobilinuria is as apt to occur in normal as in toxemic pregnancy. This has not been our experience in this study. Two reasons may account for this: first, previous work has utilized the dilution method for the detection of urobilin, a method which is not accurate; second, this former work presents little of a clinical nature, and there is no evidence that it was adequately controlled. In the vast majority of nephritic patients and controls studied in this series urobilin was either absent or present in normal quantities. Sharply differentiated from these two classes were the results obtained in the other toxemias where urobilinuria was found in greater degree, and it was found consistently.

Certain studies were made on the quantitative determination of urobilin in the blood. No previous work in this field in pregnancy could be found in a careful review of the literature. Royer finds that the concentration of this substance in the urine varies as its concentration in the blood. Nothing is actually known of the renal threshold of urobilin. In this series there was no apparent relation between the concentration in the blood and urine.

Microscopic study of hepatic and renal tissue is not available during the treatment of pregnancy toxemia, and it is common experience that the differential diagnosis of the type of toxemia is difficult. If it were possible to employ a simple laboratory test to help make this diagnosis, another aid in treatment and prognosis might be afforded.

The cases, numbering 70, which form the basis of the present study were classified as follows: nephritic toxemia, preeclampsia, eclampsia, the vomiting toxemias, acute yellow atrophy of the liver.

*Nephritic Toxemia.*—Thirty-eight patients were of the nephritic type. Among the factors in making this diagnosis was a history of previous pregnancy toxemia, multiparity, continued hypertension or albuminuria during the puerperium, the relatively early onset of the toxemia, azotemia, and a grossly impaired renal function.

*Preeclampsia.*—This condition, of which 23 cases were encountered, is often difficult to diagnose. When a toxemia occurred, usually late in pregnancy, often in a primipara, accompanied by the well-known clinical symptoms and when it was believed that eclampsia would result if no treatment were given, and further, when the signs and symptoms returned to normal relatively early in the puerperium, then it was classified as preeclampsia.

*Eclampsia.*—The diagnosis presents little difficulty. It is necessary to rule out uremia, epilepsy, and other conditions with convulsive seizures.

*Vomiting of Pregnancy.*—In this series patients were noted as having pernicious

vomiting of pregnancy when, early in gestation, they continued to vomit on starvation diet, no other organic cause being demonstrable.

*Acute Yellow Atrophy of the Liver.*—Three patients with acute yellow atrophy of the liver were included. The first died, autopsy confirming the diagnosis. The second recovered, and has been reported by Rice. The third case was complicated by syphilis and the liver atrophy was due in part to arsenic.

#### DISCUSSION OF CLASSIFICATION

No subgroups were included. The hypertensive toxemia described by Corwin and Herrick frequently ends in kidney damage, and it was believed that clinically the secondary renal involvement was of greater import than the primary arterial disease.

Stander originated the classification used in this series but he included a group known as "low reserve kidney." Here a few such cases were placed in the nephritic category, as it was believed that there was a fundamental renal pathologic condition. Pregnancy has been called the most delicate test of renal function.

Obviously in such a small series as this there will be found borderline types, hard to fit exactly into any of the major classifications. Such cases were placed in the group in which they seemed best to belong clinically.

#### CONTROLS

These were carefully selected, the following qualifications being satisfied; first, at no time a systolic pressure of 130 mm. Hg or more; second, no albuminuria at any time; third, no toxic symptoms at any time. Control figures on urobilin, amino-acid nitrogen, icterus index were obtained from such selected cases simultaneously with the investigation of the toxemias. Control values for routine blood chemistry were taken from the well-established figures of Killian and Sherwin, Folin, Slemons and Morris, Caldwell and Lyle, Denis, and Harding.

#### GENERAL CONSIDERATIONS

A definite plan was adopted and each case was considered from nine points of view, the age and parity; the past history; physical examination; the period of gestation at which the toxemia began; antepartum course, including blood pressure, urinalysis, blood chemistry, and symptomatology; term, and the type of delivery; weight and condition of the baby; the placenta; the postpartum period. This paper is concerned chiefly with the first five points.

##### *Age and Parity.*—

Nephritis	28 plus years
Preeclampsia	27.5 years
Eclampsia	30.5 years
Vomiting	29.5 years
Atrophy	29.5 years

There is little shown here except that toxemias tend to occur in patients older than the average.

	PARA	GRAVIDA
Nephritis	2.55	2.5
Preeclampsia	1.33	1.33
Eclampsia	1.0	1.0
Vomiting	2.25	3.0
Atrophy	4.0	6.0

Multiparae constituted 53 per cent of the nephritic toxemia cases, but only 30 per cent of the others. In the nephritic group among 93 pregnancies there were 83 viable babies, while in the hepatic group 32 pregnancies resulted in 34 live babies.

*The Past History.*—The following conditions were considered significant in the past history: scarlet fever, diphtheria, repeated tonsillitis, rheumatic fever, kidney disease, very bad teeth, syphilis, previous pregnancy toxemia, and repeated miscarriage.

Nephritis	22 cases or	58%
Preeclampsia	6 cases or	26%
Eclampsia	No cases	
Vomiting	2 cases or	50%
Atrophy	3 cases or	100%

Of interest are 15 patients in the nephritic group who had a history of previous pregnancy toxemia, while none of the preeclamptic or eclamptic patients had such a history. One nephritic patient had had a previous antepartum eclampsia and another eclampsia postpartum. One vomiting patient had had a similar toxemia with her first baby, and one of the patients who had acute yellow atrophy of the liver had had a previous eclampsia.

*Onset of Toxemia.*—This is not always possible to determine. A number came to the clinic with toxemia already present. If the history of the onset was not clear, it was fixed at the time when the patient was first seen. The average time, in weeks, is here shown.

	AVERAGE	EARLIEST	LATEST
Nephritis	28	10	39
Preeclampsia	34.5	25	38
Eclampsia	31.5	27	36
Vomiting	9.25	4	20
Atrophy	25	4	39

The well-known fact that nephritic toxemia is apt to begin earlier in gestation than hepatic types is here clearly shown.

*Physical Examination.*—In the early toxemias there was often no objective pathology. Later marked changes were noted. In the nephritic group edema, anasarca, enlarged heart, and frequent systolic murmurs were encountered; there was one case of mitral stenosis and one of polyhydramnios; none had syphilis. In the preeclamptic group edema, muscular twitching, and eye symptoms were prominent; one patient was stuporous; one had syphilis. The patients who had eclampsia presented the typical findings. Among the cases of atrophy two patients had syphilis; two were stuporous and markedly jaundiced. One patient with pernicious vomiting had a double mitral lesion. The

retinal findings were more pronounced in those women who had nephritis, many having arteriosclerosis, tortuosity of the vessels, and one edema of the retina. One woman with impending eclampsia showed fresh hemorrhages and exudate but most of the others in this group had normal fundi.

*The Antepartum Course.*—The blood pressure and urinalysis, the clinical symptomatology, and the laboratory results were studied.

It is impossible to present graphically the blood pressure readings, but these were taken frequently, by the same observer. In the majority of instances there was a rough agreement between the severity of the patient's condition and the height of the blood pressure, but this was not always so. Thus, a woman with a nephritic toxemia and a pressure of over 250 mm. Hg systolic felt well, although she delivered a macerated premature infant; another with eclampsia who had five or six convulsions at no observed time had a tension of over 140 mm. Hg systolic, although readings were taken immediately before and after several convulsive seizures. Albuminuria was present in relatively greater amounts in the hepatic than in the nephritic group.

The laboratory work embraced two major divisions; viz., studies of the urine, and studies of the blood. As has been said, the quantity of urobilin in the urine was considered important. It was found that there was less than the normal average (3 mg. per 100 c.c.) of urobilin in both the nephritic and the control series. This is in sharp contrast to the hepatic series where more than twice the normal amount is to be found. There is no apparent relation between antepartum and postpartum figures for the individual case. Thus, one nephritic toxemia patient showed 44 mg. of urobilin on the second postpartum day, this woman having the highest degree of urobilinuria in the entire nephritic series, and being of particular interest in that she had had eclampsia with her first baby.

In types of toxemia where liver damage has been thought to be most marked, the greatest amounts of urobilin were found. It is interesting to note that urobilinuria was more marked postpartum in preeclampsia than in eclampsia, possibly because liver damage was suffered over a longer time in the nonconvulsive toxemia. Very high degrees of urobilinuria were noted in vomiting patients, but the highest figures were to be found in those patients with liver atrophy who recovered. As might be expected these showed little or no urobilinuria antepartum, as the liver was presumably so badly damaged that the *anlage* of urobilin could not be excreted. Its presence postpartum can then be taken as a measure of improvement, showing that the liver is becoming "unlocked."

Those patients who showed a degree of urobilinuria higher than the normal fell into the class of hepatic toxemias with great regularity. Moreover, the nephritic toxemia patients very rarely presented any pathologic increase in the excretion of this substance.

In order to be reassured that urobilinuria was a function of pregnancy toxemia per se, separate protocols were drawn up to include those whose physical status was complicated by tuberculosis, syphilis, etc. Of these only lues, and then only when treated with arsenic, may have been the cause of the urobilinuria in 1 or 2 cases.

A series of two-hour renal function tests was done according to the method of Mosenthal. There was no demonstrable relation between impaired or normal fluctuation of specific gravity, and nitrogen retention, hypertension, or fetal mortality.

The nitrogen partition of the blood was estimated to include the NPN, the urea N, the uric acid, and in some cases the creatinine, and the amino acid N. The sugar was also studied, and in some cases the CO<sub>2</sub> combining power of the plasma, the icterus index, and the quantitative van den Bergh reactions. The quantitative determination of urobilin in the blood was done. The NPN-urea N ratio was computed. This ratio is of interest in that it has been considered of value as a differential diagnostic point between nephritic and hepatic toxemias.

A summary of the blood chemistry findings includes the following:

1. The averages of a large number of determinations are presented, and variations are slight.
2. There is a striking lack of nitrogen retention except in cases of liver atrophy with subsequent renal damage.
3. The NPN is lower postpartum than antepartum in hepatic toxemias, while the opposite is true in nephritis.
4. The urea N is absolutely very low, a fact which may be explained by its ready diffusibility in the amniotic fluid and increased blood volume.
5. The uric acid is consistently high in eclampsia and acute yellow atrophy of the liver.
6. The amino acid N, which is increased only in cases of atrophy of the liver, tends to be a little higher during the postpartum period.
7. No conclusions can be drawn from the figures on sugar, as they varied within such narrow limits.
8. The icterus index was increased postpartum in eclampsia, and was very high in liver atrophy.
9. The urobilin in the blood was below the normal average of 0.1475 mg. per 100 c.c. in all cases.
10. The NPN-urea N ratio was higher in the preeclamptic group than in the nephritic group.

*The Postpartum Course.*—For the sake of contrast all the laboratory work has been considered with the antepartum section. Of interest were the late findings in a number of patients. Six months to a year after delivery persistent hypertension was occasionally encountered in patients who had left the hospital with a normal pressure. It is important not to classify the toxemias clinically too early.

Twins were delivered twice in the preeclamptic group and once to a patient who had nephritis. There was one maternal death, a patient with acute yellow atrophy of the liver who died undelivered.

#### SUMMARY AND CONCLUSIONS

A series of toxemias of pregnancy has been studied from a clinical and laboratory viewpoint. The controls consisted of patients having normal pregnancies. Classification was made clinically, and the laboratory findings were then examined. The liver function was studied by means of the nitrogen partition of the blood and by the quantitative determination of the urobilin in the urine.

1. The routine chemistry of the blood and urine is of little value in differentiating the hepatic and nephritic toxemias of pregnancy.

2. Urobilinuria is usually not present to a pathologic degree in nephritic toxemias, but it is generally found in hepatic types.

3. Urobilinuria furnishes a further prognostic aid in differentiating these two types of pregnancy toxemia.

I wish to take this occasion to express my thanks to Dr. Hervey C. Williamson who conceived the problems studied in this paper, and under whose direction it was prepared; to Dr. Earl Brewer, who helped with the laboratory work, and to Dr. John A. Killian, under whose supervision a large part of the chemical work was done.

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### STRUMA OVARII AND INTRALIGAMENTOUS CYSTIC MYOMA EXHIBITED IN THE SAME PATIENT

REPORT OF A CASE, WITH A BRIEF COMMENT ON THESE RARE NEOPLASMS

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THE addition of another case report to a medical literature already flooded with such items must inevitably be prefaced, if not by an apology, at least by an explanation. The history which follows is considered worthy of record for three reasons: that the combination of the multiple pathologic conditions found is unusual in a single patient; that struma ovarii and intraligamentous cystic myoma are, according to the literature, decidedly rare tumors and seem never to have been reported in association; and that the patient's history exhibits some very remarkable features, chiefly the recurrent attacks extending over a period of many years and finally brought to an acute stage by a complete revolution of the pedicle of the strumous ovarian growth.

Mrs. L. C. S., a white woman thirty-five years of age, was admitted to Touro Infirmary July 25, 1931, complaining of sharp pain in the right lower quadrant of the abdomen, associated with nausea and vomiting. For the last five years she had suffered at monthly intervals with attacks of a similar character, which, however, were not related to menstruation. The pain was always of a stabbing quality and so severe that it frequently had to be relieved by morphine, and nausea and vomiting were always associated. The acute attack usually lasted twenty-four hours, and the abdomen remained sore for three or four days afterward. The recurrent ill-

nesses naturally brought about a chronic condition of weakness and exhaustion, and there was a story of a considerable loss of weight.

On May 29, 1931, about two months before the patient was admitted to the hospital, the periodic attack of pain persisted for a week instead of for the usual twenty-four hours, and the abdominal soreness lasted for ten days instead of the usual three or four. In addition, the nausea and vomiting were more pronounced than in previous attacks, and some fever was present for two days. No further attacks occurred until July 19, six days before admission, when she had a sudden attack of dizziness, followed by fainting; weakness and nausea persisted after she regained consciousness.

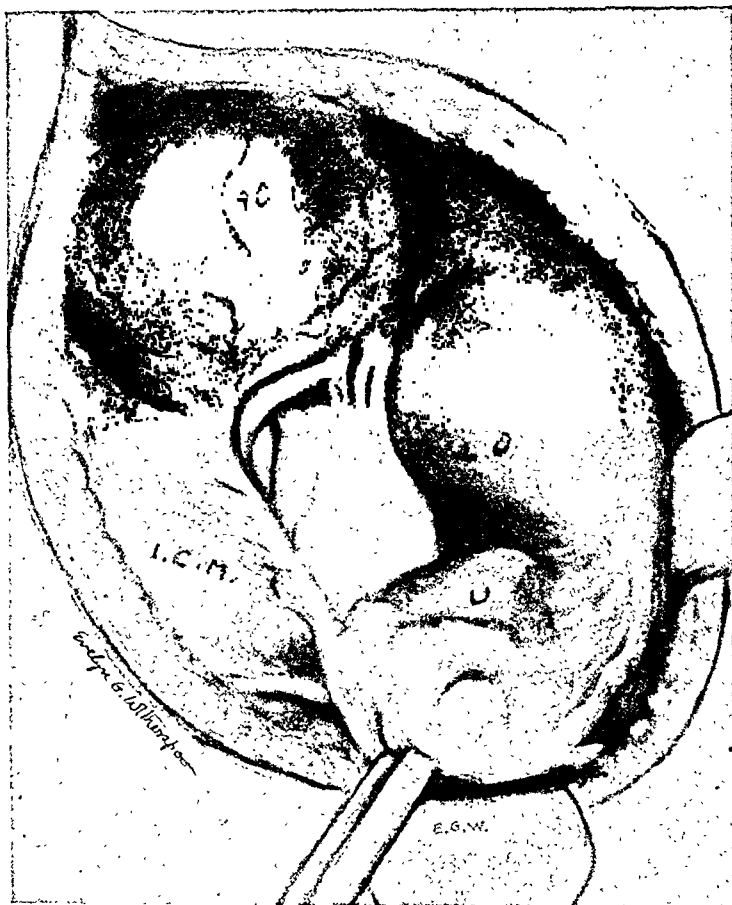


Fig. 1.—Extended McBurney incision. *U*, uterus studded with myomas; *L. O.*, dermoid cyst of left ovary; *R. O.*, struma ovarii of right ovary with twisted pedicle; *I. C. M.*, intraligamentous cystic myoma in right broad ligament, extending under right tube posteriorly.

The usual pain did not occur until the following day, but then was of such severity that she was forced to cry out for assistance, and only a large dose of morphine brought relief. All the symptoms, pain, nausea, and vomiting, persisted, unaffected in any way by the daily bowel movement; the temperature ranged between 100° and 101° F., and weakness was progressively more marked. When the patient was finally brought to the hospital by her local physician, after a trip of thirty-odd miles by automobile, she was greatly weakened and exhausted.

*Previous History.*—In most respects the family and past history seemed to have no bearing on the present condition. There was no history of hyperthyroidism in the family, the patient being questioned on this matter after operation, when the nature



of the ovarian tumor had been discovered. Menstruation was normal in regard to onset, flow and periodicity, though cramping pains were regularly present on the first day. The recurrent attacks of pain, as has already been noted, apparently had no influence whatsoever upon any aspect of menstruation, and the usual type of period had occurred some two weeks before admission to the hospital. For some ten years the patient had suffered with chronic constipation which was relieved only by frequent and rather strong laxatives. Her two deliveries were without incident except that at the second, three years ago, she had been told that she had a right-sided pelvic tumor, and since then it had been suggested to her at intervals that a possible rupture of this growth could account for her attacks of pain and the associated symptoms. Until the present time she had consistently declined surgical intervention.

Examination showed a thin, pale woman, who looked feverish and ill and who seemed to be in acute abdominal distress. Temperature on admission 100.6° F., pulse 120, blood pressure 120/80. The general examination was negative, and investigation of the thyroid after operation showed no enlargement. The distended abdomen was generally tender, but localized pain was noted only over McBurney's point; in this area there could be palpated a definite and very tender mass, the exact limits of which could not be determined. Pelvic examination revealed a parous cervix and a uterus one and a half times its normal size, which was studded with small myomas and which was firmly fixed in the normal anterior position. In the right broad ligament and in the culdesac there could be palpated a mass apparently connected with the uterus, which it seemed to be holding in the anterior position, but it was too low, too firmly fixed and not nearly tender enough to be considered as the same mass which had been palpated abdominally. Further pelvic examination was impossible because of the patient's acute discomfort.

The urine was normal except for the presence of acetone (two plus). No other laboratory examinations were made, as the patient's condition was apparently too acute to warrant further delay and immediate surgical intervention was clearly indicated.

A preoperative diagnosis of appendiceal abscess, associated with uterine myomas, seemed entirely reasonable, though ruptured ectopic pregnancy and torsion of a pedunculated uterine or ovarian tumor were also considered as possibilities. The postoperative diagnosis, however, proved to be multiple uterine fibroids, right intra-ligamentous cystic myoma, bilateral dermoid cysts of the ovary, chronic periappendicitis, and chronic cholecystitis.

*Operation.*—Operation was undertaken with the idea of rectifying only the supposed acute abdominal disease, which was considered to be located in the appendix, and for that reason a McBurney incision was made. The choice proved to be unfortunate, for before the operation could be concluded the wound had to be enlarged in both directions to permit the removal of the uterus and the adnexa, and exposure was by no means as simple as it would have been through another approach.

Successive revelation of the various conditions present within the abdominal cavity was remarkably interesting. As soon as the abdomen was opened there was seen at the lower angle of the incision a very soft mass, which lay apparently within the right broad ligament and completely beneath the peritoneum, while at the upper angle there appeared a hard, purplish, hemorrhagic structure which was surrounded by a fibrinous exudate and which extended downward and was adherent to the soft tumor just described. The upper mass at this time was considered, chiefly because of its color, to be the under surface of the liver, though its relation to the gall bladder could not be determined because the latter structure could not be identified.

As soon as the urinary bladder had been located and had been ruled out from the soft broad ligament mass, this tumor was enucleated by incision through the peritoneum of the broad ligament, and its uterine attachment, which was just then discovered and through which it apparently received its blood supply, was severed.

Examination after removal showed it to be an intraligamentous myoma undergoing cystic degeneration.

Since the acute symptoms quite evidently could not be attributed to this neoplasm, further investigation was undertaken, and because the uterus was studded with multiple myomas, supravaginal hysterectomy was decided upon. As soon as it had been brought up into the wound by clamps applied to the inner aspects of the broad ligaments, another tumor, which proved to be a dermoid cyst of the left ovary, was revealed in the culdesac. Left salpingo-oophorectomy was done, and supravaginal hysterectomy was completed by the usual technic. Peritonealization was satisfactory, although the closure of the large raw area left after the enucleation of the intraligamentous myoma was not altogether easy.

When the pelvic work had apparently been completed, attention was directed to the structure which had been assumed to be the liver, but which now proved, on further investigation, to be a dermoid cyst of the right ovary whose pedicle had undergone one complete revolution. The torsion of this tumor unquestionably was responsible for the acute abdominal distress. When it had been removed, together



Fig. 2.—Microscopic section of struma ovarii, presenting thyroid tissue with colloid formation. Basal epithelial layer seen at edge of section.

with the right tube, the appendix, which had been lying beneath the mass, came into view. It was not intrinsically diseased, but was involved in a definite periappendiceal inflammation, which did not, however, seem to warrant its removal in view of the extensive nature of the surgery already done. Examination of the gall bladder showed it to be quite small and chronically inflamed; the wall was much thickened but no stones could be palpated. It was left undisturbed, and the wound was closed by the usual layer-to-layer approximation, without drainage. Because of the length of the incision four retention sutures were inserted.

It is impossible adequately to describe the distortion of the abdominal contents which this patient presented; a systematic exploration, with an orderly consideration of the measures to be taken, was entirely out of the question, and the procedure was literally a step-by-step performance, necessitated by the exigencies of the case as one complication after another presented itself.

*Pathologic Report.*—The pathologist's report (Dr. John A. Lanford) showed both tubes to be normal except for a fibrinous exudate on the right side. The uterus was studded with multiple interstitial and subperitoneal fibroid tumors. The report on the intraligamentous myoma and the ovarian tumors is considered sufficiently interesting to be quoted in detail, and it is herewith given:

"The intraligamentous myoma measures 16 by 8 by 10 cm., and it apparently had some connection with the uterus, for at one point it shows tissue which seems to have been excised from that organ. On section the myomatous tissue seems flabby, and there is one large area of cystic degeneration. While there are many small, firm areas, well encapsulated and arranged in whorls, the structures as a whole seem to be waterlogged.

"The right ovarian mass measures 12 by 6 by 6 cm. It is nodular in its make-up, with a fairly firm external surface of purplish-red color. It has a fluctuant feel in some areas, in others it is quite firm. On section it is multilocular, and teeth, hair, thyroid tissue and blood clots appear as its chief components. The cyst of the left ovary measures 12 by 6 by 6 cm., and is rather irregular in shape. It is grayish-white in color and is quite fluctuant on palpation. On section the wall exhibits the histologic structure of a multilocular cyst. The contents are creamy and cheesy, and quantities of hair are also present.

"The pathologic diagnosis is chronic perisalpingitis; dermoid cyst of the left ovary; teratoma of the right ovary in which thyroid tissue is marked (struma ovarii); right intraligamentous cystic myoma; myomata uteri."

The patient's recovery was without incident and she was discharged in excellent condition on the sixteenth day after operation. Four months later, she was perfectly well and strong, had regained much of the weight she had lost during her long illness, and exhibited no hernial weakness in her wound.

#### COMMENT

The origin of mixed ovarian tumors affords a tempting field for speculation, but such a discussion has no place in a purely clinical report. The constitution of such tumors, on the other hand, cannot be ignored because of the part the histology plays in fixing the nomenclature of these growths. Wilms, as long ago as 1895, showed that the term dermoid, as usually applied to ovarian cysts, was a misnomer which had arisen from an erroneous conception of their structure, then generally considered to be a simple ectodermal formation. At the same time, on the ground that all ovarian dermoids contain the three germinal layers, he advanced the dictum that there exist in the ovary no tumors composed only of skin. It was his opinion that the cystic type of dermoid should be termed embryoma and the solid type teratoblastoma. Somewhat later Pfannenstiel, who accepted Wilms' conclusions, made the additional point that ovarian dermoids or cystic tumors differ from ovarian teratomas or solid tumors chiefly because dermoids exhibit elements partially or completely recalling fetal or adult organs of the human body, and so are benign, whereas teratomas exhibit elements of the three germ layers growing with unrestrained license and exhibiting a cell structure atypical in form, size, and arrangement, and so are malignant.

At the present time the tendency is to refer to both cystic and solid ovarian tumors as teratomas, but to distinguish them on the basis of their physical characteristics. A cystic teratoma or dermoid of the ovary is defined as a tumor arising from all three fetal layers, in which the tissues are arranged in a more or less orderly fashion, and in which the structures arising from a single tissue type, the ectoderm, are usually predominant. Askanasy has offered the explanation that the elements

of the other fetal layers have either completely atrophied or have undergone a suppressed development, and in the absence of a more reasonable theory his hypothesis may be accepted. A solid teratoma of the ovary is defined as a tumor which likewise arises from all three germinal layers, but in which the tissues are mingled together indiscriminately and represent for the most part an embryonic development; on microscopic examination all the tissues of the body are found scrambled together and growing in an utterly lawless manner. Clinically, the chief point of interest is that, as would be expected, the dermoid tumor is benign, while the teratoma or disorderly tumor is highly malignant.

Graves, from whose scholarly discussion much of the foregoing material is quoted, declines to accept the present nomenclature absolutely. He seems to feel that the term "dermoid of the ovary" is firmly established in medical usage and conveys a perfectly definite meaning, for throughout the fourth edition of his text he continues to use it as a synonym for what he calls "the clumsier though more scientific term, cystic teratoma." For that matter, it is interesting to note in the literature that practically all the authors who seek a meticulously scientific designation of these teratoid tumors always, when they wish to make themselves perfectly clear, revert to the old terms dermoid and teratoma. The general impression that a tumor diagnosed as a teratoma is a tumor that is malignant is excellently illustrated by the sequence of events in this special case. The pathologist, perfectly scientifically and perfectly correctly, reported the specimen as a teratomatous tumor. The surgeon in charge of the case was perfectly aware of the new nomenclature, but practically, when it came to the test, he forgot it altogether, and he promptly sought out the pathologist, to inquire of him his ground for reporting a grossly benign dermoid cyst of the ovary as a highly malignant neoplasm.

A study of the literature reveals the fact that to date only 50 cases have been reported of struma ovarii, the type of tumor in which thyroid tissue is the sole or chief constituent, though thyroid tissue in small quantities is a fairly uniform finding in dermoid growths. Pick, in 1902, first advanced the theory, now rather generally accepted, that struma ovarii is a one-sided teratoma in which the thyroid anlage has dominated or completely supplanted the elements of the other germ-layers; the older idea was that thyroid tissue in such a location was metastatic and therefore malignant, which is not a very reasonable supposition in view of the fact that thyroid metastases are usually to bone. Pick felt that the significance of such tumors was the same whether they contained large or small amounts of thyroid tissue, and up to the present time it has never been established just what quantity must be present to justify giving to the tumor the designation of struma ovarii. In many reported cases the thyroid element is represented by small isolated and discrete nodules, although in other instances it constitutes the bulk of the tumor. When the thyroid tissue forms only part of the neoplasm, the other con-

stituents may include, either singly or in combination, skin, hair, cartilage, intestine, teeth, and sebaceous, sweat, and salivary glands.

The cystic type of struma ovarii has characteristics similar to those of the pseudomucinous ovarian cyst, but its colloid contents can be differentiated from the pseudomucin of the latter growth both morphologically and chemically. Solid strumous tumors are more cellular than the cystic type, and they tend to invade the surrounding tissues and to metastasize freely. Ewing is of the opinion that the so-called solid ovarian cancer may be a tumor of this type in which the thyroid elements have lost their distinctive characteristics.

Why thyroid tissue should develop in the ovary has never been established, and the theories advanced are not entirely satisfactory. Kretschmar's idea is ingenious, that it has the same origin as the hypertrophic tissue of a true thyroid tumor, but against it is the relative infrequency of strumous tumors as opposed to the decided frequency of goiters, as well as the fact that these neoplasms are no more frequent in the endemic goiter belt than they are in other localities. While some strumae ovarii contain iodine, its absence does not nullify the diagnosis, since it has been frequently pointed out that the fetal thyroid gland is normally lacking in this chemical element.

From the reported cases of struma ovarii certain clinical facts (Frankel and Lederer) may be gathered. These tumors are most frequent in women over forty years of age; they have been noted as early as twenty-two and as late as fifty-seven years of age. They vary in their rate of growth, and they seldom cause symptoms until their size or their location introduces the factor of mechanical pressure. Then constipation, retention of urine, and prolapse of the vagina are noted. Ascites was present in some 50 per cent of the reported cases, although malignancy was noted in only a few instances. Strumous tumors usually have a pedicle. They vary in size and shape, and they may be cystic or solid.

In 11 of the 50 reported cases thyroid tissue made up the whole tumor, but in only 2 cases was an associated goiter present. Kovács' patient presented a very interesting history, the subsidence of definite symptoms of exophthalmic goiter after excision of the ovarian growth. Trapl's case (Graves) suggests that a strumous tumor of the ovary may function vicariously for the thyroid gland itself. In one of Rohdenburg's cases an ovarian fibroma was associated with the struma ovarii.

The subject of intraligamentous cystic myoma has recently been thoroughly studied by Vidrine and D'Aunoy, who have collected 6 cases from the literature and who add to this group a case of their own. The records of Charity Hospital (New Orleans), according to these authors, reveal no case of this sort, and they quote Kelly and Cullen to the effect that none was noted in the 1600 cases of myoma uteri which they personally studied. The rarity of such growths is rather astonish-

ing; intraligamentous myomas are frequently encountered in pelvic operations, and while cystic changes are relatively rare in fibroids, they do occur, so that the association of the two conditions would seem, on the face of it, not to be unusual. A similar tumor, it might be remarked in passing, was found in a patient operated upon by C. Jeff Miller some months ago, but was not put on record.

The tumor in the case which is herewith reported was on the right side, and it is probably merely a coincidence that in all the cases heretofore reported it occurred on the left. The relations between the broad ligament mass and the uterus vary, as Vidrine and D'Aunoy point out, from almost complete isolation to a rather intimate connection, which probably represents the blood supply of the tumor. Eden, with whom Smith agrees, considers that this connection between the two structures rather strengthens the theory that such tumors originate from the uterus rather than from the smooth muscle tissues of the broad ligament. Failure to identify and isolate the ureter as it crosses over the top of the tumor may result in serious damage to it as extirpation of the cyst is proceeded with, but in other respects the operation is seldom difficult, chiefly because the myoma is usually well encapsulated.

#### SUMMARY

1. A case is reported in which there was exhibited, in addition to a dermoid cyst of the left ovary, multiple uterine fibroids, chronic periapendicitis, chronic perisalpingitis, and chronic cholecystitis, two rare pathologic conditions, intraligamentous cystic myoma and struma ovarii, the latter tumor presenting also a twisted pedicle which caused acute abdominal symptoms.

2. The nomenclature of cystic and solid teratomas of the ovary is discussed.

3. Struma ovarii is considered in its clinical aspects as they are set forth in the 50 cases reported in the literature.

4. The 7 cases of intraligamentous cystic myomas reported in the literature are briefly reviewed.

I am indebted to Dr. C. Jeff Miller for the privilege of reporting this case, which occurred on his private service at Touro Infirmary.

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## THE FOTHERGILL OPERATION FOR THE CORRECTION OF UTERINE PROLAPSE, WITH A REPORT OF END-RESULTS\*

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FOTHERGILL, of Manchester, after years of work, finally developed a standardized operation for the radical cure of uterine prolapse. Those who adopt his technic will have at their disposal a safe, simple and anatomically correct procedure, which gives uniformly permanent cures in approximately 100 per cent of the cases.

It is quite probable that this method of surgical treatment of prolapse will remain unchanged for some time to come, since the permanent results are as good as can be expected of any operative method.

The success of Fothergill's method stands out in marked contrast to the earlier procedures. Recurrences were all too frequent after vaginal work alone, although attended by improvement when combined with abdominal suspension or fixation, and whereas the interposition operation gives a higher percentage of successes than the vaginoabdominal operation, it is limited in its scope and is anatomically and physiologically unsound.

Clinical experience and anatomic research taught Fothergill that the pelvic viscera are not so much kept in their normal positions by being suspended from above or propped up from below, but that the uterus, vagina, and bladder are mainly held in place by combinations of unstripped muscle and connective tissue attached to the sides of the cervix and vagina. The overstretching of these structures, commonly known as the parametrium and paracolpium, is the chief contributing factor in the production of genital prolapse.

Based upon this information, Fothergill in 1907 advocated, before the Edinburgh Obstetrical Society, a method of anterior colporrhaphy in which the incision was carried well up and out on either side of the cervix, fully exposing the paracolpium and part of the parametrium, so that the closure of the wound brought together in front of the cervix structures which were formerly at its sides. Thus the cervix was carried upward and backward into the hollow of the sacrum, leaving the uterus in a position of anteversion.

This procedure sufficed for those patients in whom the cervix was not elongated. Subsequently, in 1913, he found that by carrying the vaginal incision around behind the cervix, instead of in front of it, anterior colporrhaphy and amputation of the cervix could be conveniently combined in a simple, one piece operation, instead of being done separately and in a series.

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\*Read at a meeting of the Obstetrical Society of Philadelphia, December 3, 1931.

This procedure not only saves time and trouble, but fully exposes the parametrium as well as the paracolpium. When the wound is closed, the stump of the cervix passes backward and upward and the uterus is left in its normal position of anteversion.

The appreciation of retroversion as a causative factor in the production of recurrences, led to the combining of abdominal suspension or fixation with vaginal procedures in the treatment of prolapse. However, the risk is immediately increased, and the convalescence lengthened once the abdomen is opened.

Fothergill's method eliminates the abdominal operation, and it cures the worst cases of uterine prolapse by vaginal surgery alone. Furthermore, this treatment is applicable to women of all ages, since the retention of a uterus with a three-inch canal permits pregnancy to go on to term.

Any operation for the correction of genital prolapse which leaves a rectocele uncorrected, especially if there is an accompanying prolongation of Douglas' culdesac, is courting trouble for the future. We believe that our method of procedure for its correction has added somewhat to our successful results. We remove a long narrow triangle of vaginal wall, whose apex is high up just behind the cervix, while its base curves along the margin of the perineum. In the patients in which Douglas' culdesac is prolonged we ligate the sac as high up as we conveniently can. In closing the apex of the triangle we use the Kelley figure-of-eight suture, which when tied forms a natural cup-shaped posterior fossa. The remaining closure of the wound is made with a combination of superficial and deep interrupted sutures of No. 3 thirty-day chromic catgut. Our aim is not to have too narrow a vaginal canal. Indeed, when we have completed the procedures we are able to introduce at least one finger comfortably into the vagina as far back as the cervix.

#### TECHNIC OF THE OPERATION

1. *Prolapsus With Short Uterus and Healthy Cervix, With or Without Cystocele.* (Fig. 1.) Pull down the cervix with a volsella and pick up with forceps to points in the lateral fornices directly right and left of the os externum, and about three inches apart. Push the cervix back into the hollow of the sacrum and see if the forceps will come together in front of it without undue tension. If they approach each other too easily, move them wider apart. If they will not meet, move them nearer together, and so on until suitable points in the lateral fornices are found. Pick up a third point half an inch behind the urethral orifice. Cut through the whole thickness of the vaginal wall between the three pairs of forceps so as to mark out a triangle with its base just in front of the cervix, and its apex just behind the urethra. (Fig. 2.) Separate and remove the triangle of vaginal wall. Close the wound from side to side with interrupted catgut sutures. The first suture is passed just in front of the cervix, in the center of the base of the triangle, which is pulled first into a diamond-shaped figure and then into a median line as the suturing from above downward proceeds. (Fig. 3.) All but the first three or four sutures must be tied with the uterus pushed well up into the vagina. (Fig. 4.) The cervix



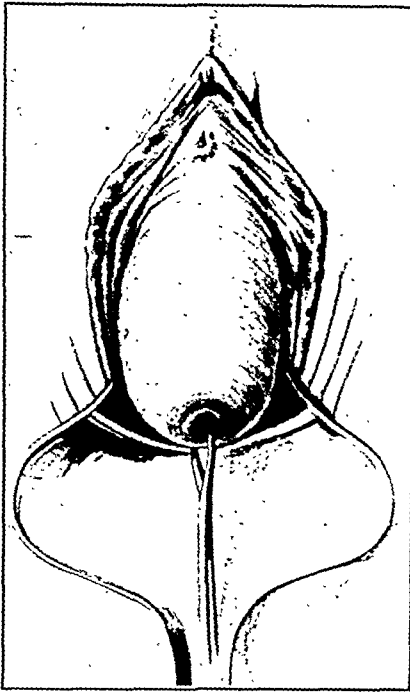


Fig. 1

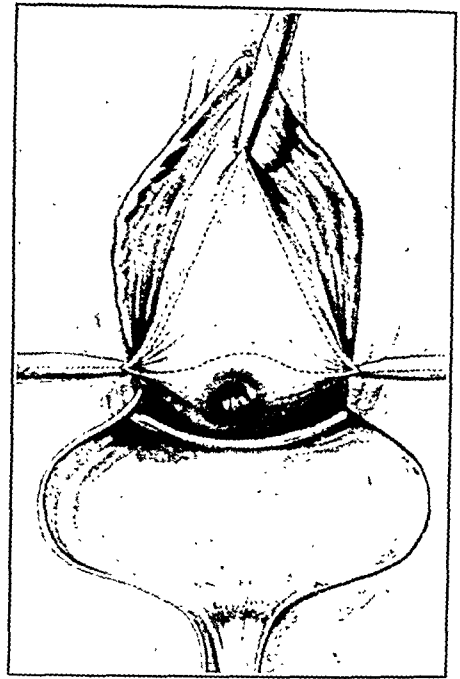


Fig. 2

Fig. 1.—Prolapsus exposed for operation. (Eden and Lockyer, *New System of Gynecology*. By courtesy of The Macmillan Company.)

Fig. 2.—Operation for prolapsus. Incision for anterior colporrhaphy without amputation of cervix. (Eden and Lockyer. By courtesy of The Macmillan Company.)

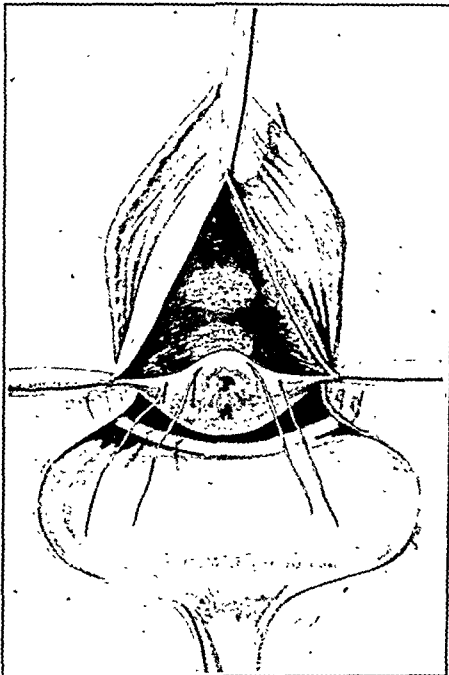


Fig. 3

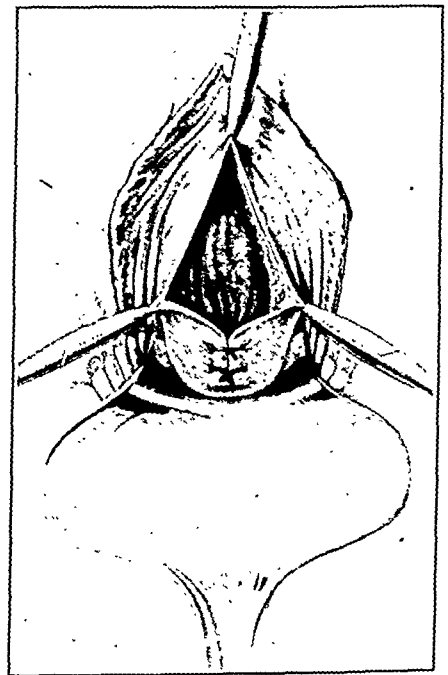


Fig. 4

Fig. 3.—Operation for prolapsus without amputation of cervix. Triangle of anterior vaginal wall removed to expose parametrium and paravaginal tissue. The first and second sutures are shown. (Eden and Lockyer. By courtesy of The Macmillan Company.)

Fig. 4.—Operation for prolapsus without amputation of cervix. As the incision is closed, the cervix disappears upward and backward. For purpose of illustration it is here shown pulled more downward and forward than it is in practice. (Eden and Lockyer. By courtesy of The Macmillan Company.)

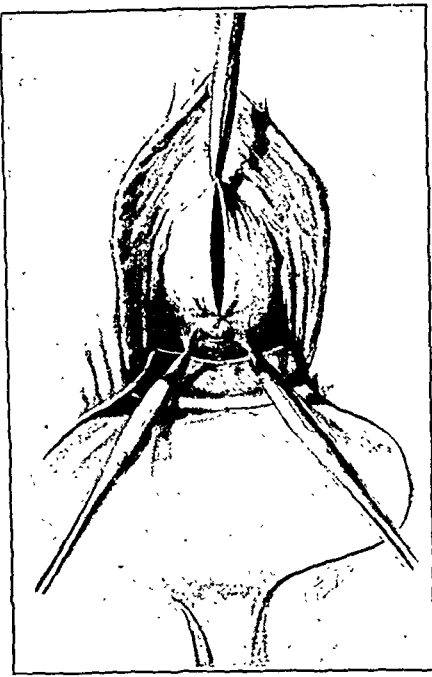


Fig. 5

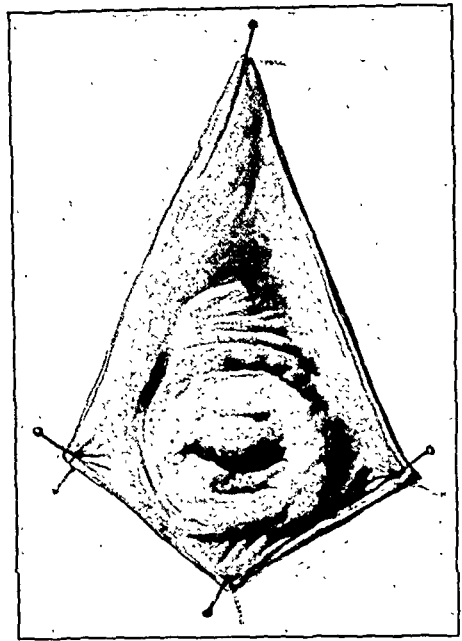


Fig. 6

Fig. 5.—Operation for prolapsus. The cervix has disappeared and lower part of incision is held forward by forceps for purposes of illustration. (Eden and Lockyer. By courtesy of The Macmillan Company.)

Fig. 6.—Operation for prolapsus by amputation of the cervix, combined with anterior colporrhaphy. The specimen consists of the portion of vaginal wall removed together with the cervix. (Eden and Lockyer. By courtesy of The Macmillan Company.)

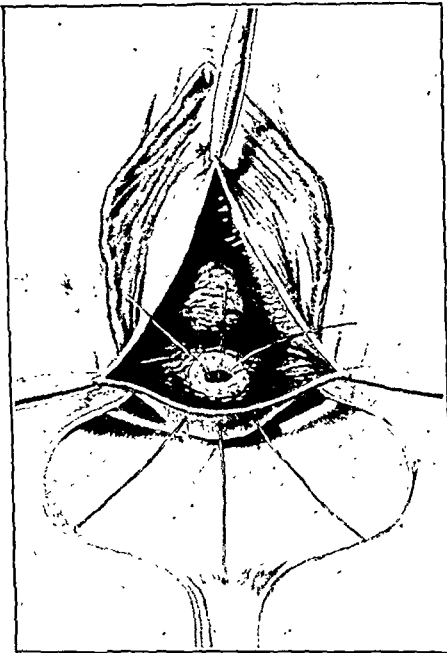


Fig. 7

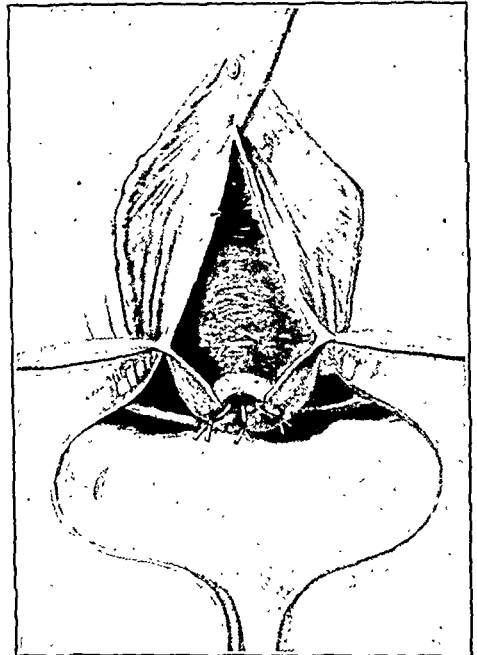


Fig. 8

Fig. 7.—Operation for prolapsus by amputation of the cervix, combined with anterior colporrhaphy. The incision is made, the vaginal wall and cervix have been removed, and the first three stitches inserted. (Eden and Lockyer. By courtesy of The Macmillan Company.)

Fig. 8.—Operation for prolapsus by amputation of the cervix combined with anterior colporrhaphy. The first three stitches are tied. (Eden and Lockyer. By courtesy of The Macmillan Company.)

should disappear from view as the lower sutures are inserted and tied. (Fig. 5.) This operation alone would cure prolapse without any repair of the perineum. But the vagina should be restored to its normal size, shape and position. Perineorrhaphy by a good method should always be done, after bleeding from the anterior colporrhaphy wound has been checked, if necessary, by the insertion of extra sutures.

2. *Prolapsus With Long Uterus or Unhealthy Cervix, With or Without Cystocele. Anterior Colporrhaphy With Excision of the Anterior Fornix Combined With Amputation of the Cervix in One Piece. Perineorrhaphy.* Pull down the cervix with a volsella, dilate it, curette and measure the length of the uterine cavity, thus ascertaining how much cervix will have to be removed in order to leave a uterine cavity three inches long.

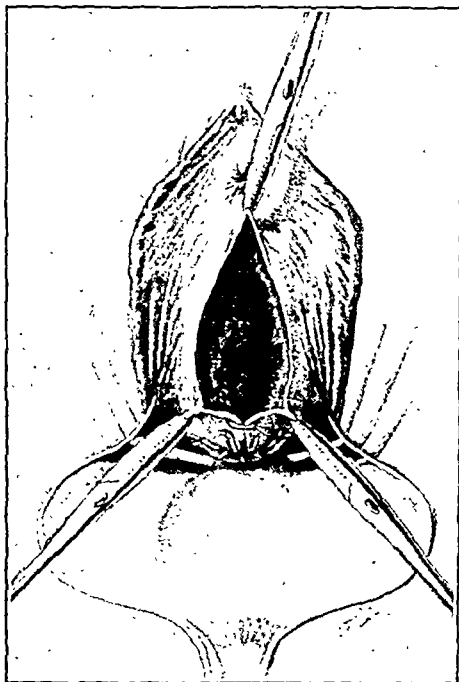


Fig. 9

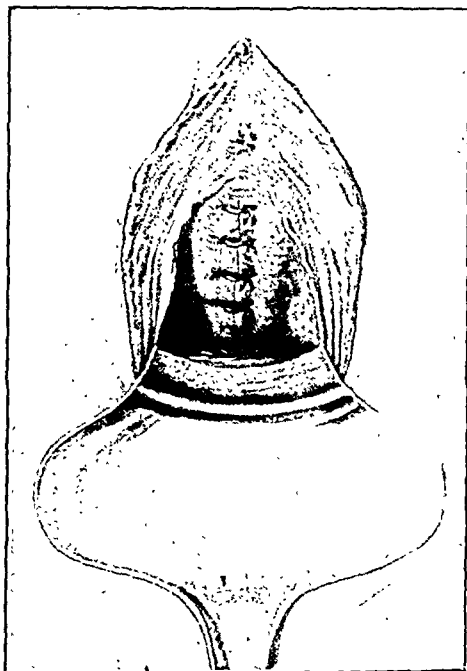


Fig. 10

Fig. 9.—Operation for prolapsus by amputation of the cervix combined with anterior colporrhaphy. The suturing of the new os uteri is completed, and the first stitch from side to side has been inserted. (Eden and Lockyer. By courtesy of The Macmillan Company.)

Fig. 10.—Operation for prolapsus by amputation of the cervix combined with anterior colporrhaphy. The suturing of the wound completed, showing that the stump of the cervix and the upper part of the wound have disappeared from view. (Eden and Lockyer. By courtesy of The Macmillan Company.)

Pick up the vaginal wall at two points in the lateral fornices directly right and left of the os externum (or even a little behind it) and about three inches apart. Apply another pair of forceps half an inch behind the urethral orifice, and a fourth behind the cervix at the cervicovaginal junction in the middle line. Cut through the vaginal wall so that the incision joins the four pairs of forceps and marks out for removal a quadrangular area with two long sides in front and two short sides behind. (Fig. 6.)

Strip off this quadrangle of vaginal wall from the urethra, bladder, and parametric tissue, working from below upward until it remains attached only around the cervix. Then, pulling up the flap of vaginal wall snip round and round the cervix until a sufficient portion of it is set free. Then cut straight across the cervix so as to leave the uterus with a cavity three inches long. The amputated portion of the cervix thus comes away in one piece with the quadrangle of the vaginal wall.

Pass the first suture of hardened catgut into the cervical canal in the midline behind, and bring it out through the vaginal wall in the midline behind. (Fig. 7.) Tie this and insert the second to the left of it so as to unite cervical mucosa and vaginal wall. Tie this and insert the third to the right of the first. (Fig. 8.) The fourth is on the left, the fifth on the right, and so on, until the cervical stump is covered, and the new os externum is surrounded by vaginal wall. (Fig. 9.)

Next insert a suture through both vaginal edges of the wound and bring them together in front of the cervix. In order to tie this suture without tension, the stump of the cervix should be within the vagina, and should be pushed up and back toward the hollow of the sacrum. The remaining sutures are passed from side to side through the cut margins of the vaginal wall, and are inserted in a series from above downward. (Fig. 10.) They are tied inside the vagina, and as the sides of the wound come together, the stump of the cervix, with the upper part of the line of sutures, passes completely out of sight upward and backward. For this reason bleeding should be checked as the suturing proceeds, for once the lower sutures are tied, the upper ones cannot easily be brought down into view again.

This operation leaves the uterus in a position of anteversion, and repair of the perineum is not required to cure the prolapse. But it is desirable to restore the natural size, shape, and slope of the vagina, for a defective perineum is a reparable accident favorable to the recurrence of prolapse. Therefore the operation should be completed by repairing the perineum.

In 1921, Fothergill published the end-results of 156 operations which were done in 1914, 1915, and 1916. These patients were traced, and as far as possible, examined. Of these 150 stated without qualification that they were cured, while 6 did not; but of these 6, 2 were found on examination to be free of anatomic prolapse, which gave a percentage of 97.3 of permanent cures. Twenty-six of his patients had 30 children subsequent to their operations, and of these 26, 23 had had their cervixes amputated. Of the 30 labors 23 were natural and 7 were instrumental.

We are able to report a total of 138 of our own patients operated upon between 1918 and 1930. Of these 113 were traced by questionnaire, the majority of whom were also examined. Persistent effort was made to trace the others but they could not be located. Of the 113, 111 stated without qualification that they were cured; 2 stated that they were not. This gives 98 per cent definitely cured. Of the 113 patients traced, 47 were in the childbearing age, and of these, 11 had 13 children and one had a miscarriage subsequent to the operation. Ten of these labors were normal and 3 were instrumental. Of the 12 who had had labors, in 10 the cervix had been amputated.

In our series there were 5 nullipara who had uterovaginal prolapse with inversion of the vaginal walls. In Fothergill's classification there were 32 cases of this type. It is well known that this form of prolapse is a most difficult type to cure.

In conclusion, we believe that the high percentage of cures obtained in our cases would alone justify this publication. Our dominant pur-

pose, however, in bringing this subject to the attention of the profession, is to awaken our colleagues to a keener appreciation of the value of an operation, which should long since have been universally adopted as the standardized operation for the treatment of genital prolapse.

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716 MEDICAL ARTS BUILDING.

(For discussion, see page 293.)

## A STUDY OF (FETAL) MORTALITY\*

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(From the Department of Obstetrics of the University Hospital)

THIS study was undertaken to determine the fetal mortality rates obtained by various methods of delivery in series of comparable cases and consists of an analysis of the 2635 cases delivered in the University Hospital Maternity Department between January 1, 1927 and November 1, 1931. Among these cases there were 230 fetal deaths, 42 between the eighteenth and twenty-eighth weeks of pregnancy which were eliminated from further consideration because of prematurity entirely incompatible with extrauterine life, and 188 cases of fetal death in deliveries beyond the twenty-eighth week of pregnancy. This gives us a fetal mortality rate of 7.13 per cent corrected only for prematurity below twenty-eight weeks of pregnancy. A review of the literature shows such widely varying fetal mortality rates based upon such markedly different standards that to quote mortality rates alone without analyzing the cases on which such rates are based would be useless and, in fact, misleading. For example, DeLee quotes a fetal mortality rate of 3.38 per cent at the Chicago Lying-in Hospital in 16,157 babies weighing over 1500 gm. The fetal mortality rate for Paris is 9.0 per cent; Glasgow 13.6 per cent, and Edinburgh 11.5 per cent. It is scarcely conceivable that these marked differences in fetal mortality rates are due alone to varying degrees of skill and judgment among the various obstetricians concerned.

From the standpoint of time of fetal death, we find there were 68 antepartum, 49 intrapartum, and 71 neonatal deaths in our series of cases. It should be stated that all babies who showed any sign of life after delivery and died within the first ten days of life are classed as neonatal

\*Read at a meeting of the Obstetrical Society of Philadelphia, December 3, 1931.

deaths. In as much as the method of delivery can have no influence on the outcome of a case in which the fetus is dead before labor begins, I have corrected all the rates to be given, by the elimination of the cases of antepartum death.

A study of Table I shows a group of 59 cases of death of the fetus due to traumatism. This entire group may be considered as preventable deaths under perfect conditions and perfect care. The second group of 37 cases in which death resulted from interference with the fetal circulation contains some preventable deaths and others that would be unavoidable even under the most ideal conditions. The third group of 20 cases of fetal deaths due to fetal abnormalities consists of absolutely unavoidable fetal mortalities. The remaining 72 cases are of both inevitable and preventable deaths.

TABLE I. CAUSES OF FETAL DEATH

	NO. OF CASES
Fetal Traumatism	59
A. Asphyxia	17
B. Intracranial hemorrhage	16
C. Birth injuries (unclassified)	15
D. Injuries due to disproportion	4
E. Trauma of prolonged labor	2
F. Postmaturity	2
G. Craniotomy	2
H. Fractured skull	1
Interference With Fetal Circulation	37
A. Abruptio placentae	12
B. Prolapsed cord	10
C. Knotted cord	3
D. Cord around neck	2
E. Pressure on cord	2
F. Extremely short cord causing abruptio placentae	1
G. Twist of cord	1
H. Ruptured uterus	1
I. Exsanguination	1
J. Narcosis asphyxia	1
K. Presumable effect of amytal on fetal heart	1
L. Nuchal arms causing delay in delivery of aftercoming head	1
M. Delay in delivery of aftercoming head	1
Fetal Abnormalities	20
A. Atelectasis	6
B. Hemorrhagic disease of newborn	3
C. Monsters	2
D. Congenital deformities	2
E. Hydrocephalus	2
F. Enlarged thymus	1
G. Stenosis of trachea	1
H. Stenosis of common duct	1
I. Congenital heart disease	1
J. Failure of respiratory center (5 days neonatal)	1
Prematurity	17
Toxemia	24
Syphilis	10
Placenta previa	6
Cause of death unknown	15

## POSITION AND PRESENTATION AS FACTORS IN FETAL MORTALITY

This group of cases comprised 54.34 per cent of our entire number of deliveries. The low fetal mortality rate of 1.65 per cent in the cases delivered by forceps is explained by the fact that a large percentage of these cases were simple control forceps in which death of the child would be actually inexcusable. From the practical standpoint such cases might very properly be considered as spontaneous deliveries and had this been done here the fetal mortality rates in the spontaneous and the forceps deliveries probably would have been reversed. Attention is called to the high fetal mortality rate among the cases delivered by podalic version and breech extraction.

This group comprises 12 per cent of our total number of cases. One is immediately struck by the high fetal mortality rate in occipitopos-

TABLE II. VERTEX PRESENTATION—OCCIPUT ANTERIOR POSITION

Total number of cases	1432
Fetal deaths	63
Antepartum fetal deaths	24
Intrapartum fetal deaths and neonatal fetal deaths	39
Fetal mortality	4.4 %
Corrected fetal mortality	2.77%

CHARACTER OF DELIVERY	TOTAL NO. CASES	FETAL DEATHS			FETAL MORTALITY	
		ANTE-PARTUM	INTRA-PARTUM	NEO-NATAL	UNCORRECTED PER CENT	CORRECTED PER CENT
Spontaneous	893	18	6	16	4.47	2.51
Forceps	488	4	2	6	2.45	1.65
Version	46	2	5	4	23.91	20.45
Cesarean section	5	0	0	0	0	0

TABLE III. VERTEX PRESENTATION—OCCIPUT POSTERIOR POSITION

Total number of cases	333
Fetal deaths	44
Antepartum fetal deaths	7
Intrapartum and neonatal fetal deaths	37
Fetal mortality	13.21%
Corrected fetal mortality	11.35%

CHARACTER OF DELIVERY	TOTAL NO. CASES	FETAL DEATHS			FETAL MORTALITY	
		ANTE-PARTUM	INTRA-PARTUM	NEO-NATAL	UNCORRECTED PER CENT	CORRECTED PER CENT
Spontaneous	39	4	1	2	18	8.57
Spont. Rotation						
Forceps Extract.	72	0	0	2		2.77
Manual Rotation						
Forceps Extract.	36	0	1	0		2.77
Seanzoni						
Maneuver	131	1	11	9	16.03	15.38
Version	37	1	3	4	21.6	19.44
Cesarean Section	14	1	3	1	35.71	30.77
Delivered as posterior occiput	4	0	0	0	0	0

terior positions. Without regard to the method of delivery we find a fetal mortality rate of nearly five times that of occipitoanterior positions. Our lowest fetal mortality rate was obtained in those cases delivered by waiting for spontaneous rotation of the occiput before applying forceps, which meant in most instances a low or control forceps delivery, and in those cases delivered by manual rotation and forceps extraction. Other methods of delivery instituted before spontaneous rotation had occurred gave us a decidedly higher fetal mortality rate.

TABLE IV. VERTEX PRESENTATION—OCCIPITOTRANSVERSE POSITION

Total number of cases	98
Fetal deaths	16
Antepartum fetal deaths	3
Intrapartum and neonatal fetal deaths	13
Fetal mortality	16.32%
Corrected fetal mortality	13.68%

CHARACTER OF DELIVERY	TOTAL NO. CASES	FETAL DEATHS			FETAL MORTALITY	
		ANTE- PARTUM	INTRA- PARTUM	NEO- NATAL	UNCORRECT- ED PER CENT	CORRECTED PER CENT
Spontaneous	6	0	1	2	50.	50.
Spont. Rotation						
Forceps Extract.	11	0	0	0	0	0
Manual Rotation						
Forceps Extract.	3	0	1	0	33.33	33.33
Forceps Rotation		2				
Forceps Extract.	60	(1 mac.)	0	3	8.33	5.17
Version	8	(1 mac.)	0	1	25.	14.28
Cesarean Section	5	0	1	0	20.	20.
Delivered as						
post. occiput	1	0	0	0	—	—
Craniotomy	4	0	4	0	100.	100.

The condition of high transverse arrest or occiput persistent transverse position is usually considered a difficult one to handle without rather marked injury to the fetus, yet in our series of 98 cases, we find a fetal mortality rate only slightly greater than that of occipitoposterior positions. This is due largely to the use of the Barton and the Kielland forceps and the securing of a good cephalic application rather than an oblique application such as would be the case if other forceps had been used. In most instances the Barton or Kielland forceps were used only as rotators and extraction was done with the Dewees' or Piper's axis traction forceps. Except for this one group of 60 cases delivered by forceps rotation and forceps extraction, our number of cases delivered by any one method was too small to eliminate the element of chance so that no conclusions may be drawn as to the relative safety to the fetus of any particular method of delivery.

Breech presentation, due to imperfect dilatation by the soft compressible breech, pressure on the cord after delivery of the umbilicus, and difficulty in delivery of the arms and the unmolded aftercoming head,



always endangers the life of the child and causes a high rate of fetal mortality. Our series of breech presentations is no exception to this rule. As may be seen from Table V the majority of our cases of breech presentation are delivered by decomposition and extraction of the breech as soon as the cervix is completely effaced and dilated. With us, spontaneous delivery in breech presentations occurs only in cases of precipitate delivery, usually in premature labors. Our results, as shown in Table V do not warrant a continuance of this procedure. Extraction of the breech after spontaneous delivery as far as the umbilicus has given us a very much lower fetal mortality rate. There is one point of

TABLE V. BREECH PRESENTATIONS

Total number of cases	112
Fetal deaths	24
Antepartum fetal deaths	11
Intrapartum and neonatal fetal deaths	13
Fetal mortality	20%
Corrected fetal mortality	12.62%

CHARACTER OF DELIVERY	TOTAL NO. CASES	FETAL DEATHS			FETAL MORTALITY	
		ANTE- PARTUM	INTRA- PARTUM	NEO- NATAL	UNCORRECT- ED PER CENT	CORRECTED PER CENT
Spontaneous	8	2	0	0	25	0
Simple Breech						
Extraction	33	2	0	2	11.43	6.06
Decomposition						
and Extraction	15	1	1	2	26.66	21.43
Decomposition						
and Extraction						
with forceps						
on aftercoming						
head	52	5	3	4	23.07	14.9
Cesarean Section	3	1	0	0	33.33	0
Craniotomy on						
aftercoming						
head	1	0	1	0	100	100

special significance to be learned from a study of Table V, viz., the very considerable reduction in fetal mortality in cases in which the Piper forceps have been used for delivery of the aftercoming head as compared with those cases in which the aftercoming head was delivered by the Mauriceau, Wiegand, Deventer or Prague methods. It is now the routine practice at the University Hospital for the attending obstetrician to apply the aftercoming head forceps in all cases in which delivery is not easily and quickly accomplished by the other methods and our statistics show a steady fall in fetal mortality as our experience with these forceps increases. The technic of the application of the Piper aftercoming head forceps, while not difficult, is quite different from that of the usual forceps application and must be followed closely to obtain the best results.

## ABNORMAL PRESENTATIONS

There were 47 cases of abnormal presentations in our series with a total of 10 fetal deaths. Of these 6 were antepartum and 4 were intrapartum and neonatal deaths. This gave us a fetal mortality of 21.27 per cent and a corrected fetal mortality of 9.75 per cent. Seven of the ten cases of fetal deaths were complicated by prolapsed cords.

## METHOD OF DELIVERY AS A FACTOR IN FETAL MORTALITY

The very low fetal mortality rate of 1.71 per cent in low forceps is due to the inclusion in this group of a large number of control forceps cases which for all practical purposes may be considered as spontaneous deliveries. However, it serves to emphasize the fact that it is the use to

TABLE VI. FORCEPS

Total number of cases		949				
Fetal deaths		57				
Antepartum fetal deaths		12				
Intrapartum and neonatal fetal deaths		45				
Fetal mortality		6%				
TYPE OF FORCEPS DELIVERY	TOTAL NO. CASES	FETAL DEATHS			FETAL MORTALITY	
		ANTE- PARTUM	INTRA- PARTUM	NEO- NATAL	UNCORRECT- ED PER CENT	CORRECTED PER CENT
High	84	1	11	7	22.61	21.68
Mid	332	3	9	9	6.32	5.47
Low	533	8	1	8	3.19	1.71
Corrected fetal mortality		4.8%				
Incidence of birth injuries from forceps		64—6.78%				

which the forceps are put, and not merely their application, that determines the fetal morbidity and mortality. Thus we find three times as high a mortality rate in mid forceps applications, and twelve times as high a mortality in high forceps, as in low forceps. Although I am not prepared in this paper to quote actual figures, still the statement may be accepted as a fact that maternal morbidity and mortality in forceps deliveries parallel the fetal morbidity and mortality. Table VI also shows an incidence of 6.78 per cent of birth injuries due to the use of forceps. Our conclusion is obvious. Unless there are definite indications for the early use of forceps they should be employed preferably after the biparietal diameter of the fetal head has passed the level of the spines of the ischii or has at least advanced to mid pelvis. The fetal mortality in high forceps deliveries is so high that it should be a strong deterrent to such use and when conditions warrant it, cesarean section with its much lower fetal mortality and maternal morbidity should be done instead.

## PODALIC VERSION AND BREECH EXTRACTION

This operation was performed in 156 cases with a total of 36 fetal deaths, giving us a fetal mortality of 23 per cent. There were 13 ante-

partum deaths, leaving 23 intrapartum and neonatal deaths with a corrected fetal mortality of 16 per cent. Only a small percentage of these cases truly could be called elective versions. Most of them were done for placenta previa, abruptio placentae, malpresentations, etc., so that our fetal mortality seems to us to be entirely satisfactory. Four cases in this group in which disproportion was diagnosed but which the operator considered so slight as not to contraindicate version, terminated in the death of the fetus and again point to the conclusion that cases of suspected or known disproportion ought to be delivered by cesarean section, never by version.

#### CESAREAN SECTION

A total of 129 cases showed 18 fetal deaths and a fetal mortality rate of 14 per cent. Inasmuch as six of these were antepartum deaths we had a corrected fetal mortality rate of 9.1 per cent in the 12 intrapartum and neonatal deaths. All of our fetal deaths in cesarean section were either absolutely unavoidable or were due to improper handling of the case before operation. Some of these babies might have been saved by early operation but under the conditions that existed when these patients were brought to the hospital no other method of delivery would have been any more successful. Such cases prove very definitely that cesarean section as a last resort cannot be expected to reduce fetal mortality. Early recognition of complications of pregnancy or labor which indicate cesarean section, and prompt operation are absolutely essential to a successful termination of the case.

#### EMBRYOTOMY

Eight cases of craniotomy are included in our series. Except when performed on a known dead fetus or upon monstrosities, embryotomy is a confession of improper judgment in the handling of the case. Five of our cases confirm this statement. Had the true situation been recognized and the patients sent in to the hospital early enough these five babies might have been saved by cesarean section.

#### OTHER FACTORS IN FETAL MORTALITY. TOXEMIA

In 40 of our cases toxemia was either the sole, or at least, the chief cause of fetal death. There were definite evidences of toxemia in 340 cases so that our total fetal mortality due to toxemia was 11.76 per cent. Our best results in toxemia cases were obtained in spontaneous deliveries. In agreement with the generally accepted idea that the fetus in toxemia cases stands shock and traumatism as badly as does the mother, we found that operative methods of delivery other than cesarean section increased our fetal mortality.

#### PLACENTA PREVIA AND ABRUPTIO PLACENTAE

We had a total of 40 cases of placenta previa with 5 antepartum and 14 intrapartum and neonatal deaths giving us a total fetal mortality

of 47.5 per cent and a corrected fetal mortality of 40 per cent. Thirty-nine cases of abruptio placentae with 10 antepartum and 8 intrapartum and neonatal deaths were also encountered. Our total fetal mortality in these cases was 46.15 per cent and our corrected fetal mortality was 27.58 per cent. Such small series of cases scarcely warrant drawing definite conclusions as to the relative value of various methods of delivery. However, our best results were obtained in these cases by cesarean section.

#### POSITIVE WASSERMANN CASES

A blood Wassermann test is made on every patient admitted to the Maternity department of the University Hospital and positive reactions repeated as a check. All patients with positive Wassermanns are immediately referred to the department of Syphilology for active treatment. The benefit of this plan is shown by the fact that, among 238 syphilitic mothers, a positive Wassermann reaction was present in only 28 cases in which the fetus died and of these, only 10 babies gave sufficient evidence of syphilis to warrant ascribing their deaths to this cause. This gives us a fetal mortality due to syphilis of 0.038 per cent for our entire series and a fetal mortality among syphilitic mothers of 4.2 per cent.

#### SUMMARY

A total of 230 fetal deaths occurred among 2635 consecutive deliveries on the Maternity Service of the University Hospital in the past fifty-eight months. Of these 42 were under twenty-eight weeks of pregnancy and because of such marked prematurity are not analyzed in this paper. The remaining 188 cases consisted of 68 antepartum, 49 intrapartum, and 71 neonatal deaths of the fetus. There were 118 unavoidable and 70 preventable deaths. This last group of cases is the chief object of study in this report.

#### CONCLUSIONS

Many fetal deaths are due to causes entirely beyond the control of the obstetrician.

Vertex presentations give the lowest fetal mortality. Of these the ratio of fetal mortality between occipitoanterior, occipitoposterior and occipitotransverse position is as 1:4.5:5.

Breech presentations portend a higher fetal mortality rate, it being nearly 3 times that of vertex presentations.

Compound and transverse presentations give a high rate of fetal mortality, in our series due chiefly to a high incidence of prolapsed cord.

All operative procedures, other than cesarean section, increase fetal mortality and the earlier in labor the interference is undertaken the greater is the danger of fetal death. The ratio of fetal deaths in low, mid, and high forceps is as 1:3:12 respectively. Cesarean section performed after long labor does not materially reduce fetal mortality. In

contrast with other methods of accouchement force, the earlier cesarean section is done the lower the fetal (and maternal) morbidity and mortality.

Fetal mortality in toxemia of pregnancy depends upon the same factors as in nontoxemic cases plus the effect on the fetus of the toxins circulating in the maternal blood. This latter factor is so variable and so difficult to evaluate that definite conclusions are not warranted.

Although our number of cases is relatively small, our series of abruptio placentae and placenta previa cases show that early cesarean section gives the lowest fetal mortality of all methods of delivery.

The incidence of positive Wassermann reactions in our series of cases corresponds quite closely with that reported by Williams in 1920. Our fetal mortality due to syphilis however, is very much lower due undoubtedly to improved methods of treatment devised during the past eleven years.

1900 RITTENHOUSE SQUARE.

(For discussion, see page 292.)

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## RECONSTRUCTION OF THE URETHRA\*

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VESICOVAGINAL fistula associated with partial or complete loss of the urethra, is a comparatively rare condition. Indeed, since the advent of better operative obstetrics preventing prolonged second stage labor, simple vesicovaginal fistula is seen much less frequently than in the times of Sims and Emmet and their coworkers. Repair of vesicovaginal fistula, especially if extensive and associated with much scar tissue, is a difficult operation and often disappointing in its results. In one case in this series, sixteen prior operations had been performed by experienced surgeons without success and a cure was obtained in the seventeenth attempt. George Gray Ward, in his paper on this subject presented in 1923, speaks of the difficulties to be overcome in curing extensive vesicovaginal fistulae as often appalling.

If the cure of simple fistula is often so difficult, it would seem that the additional complication of the partial or complete absence of the urethra, would present a condition so formidable as to deter a surgeon from attempting to correct the defect by plastic surgery. In 1880, Emmet reported that he had succeeded in six or seven cases in restoring the urethra, but also said he felt disposed not to waste his energy on the slim chance of success or permanent benefit from the operation.

Attempts to reconstruct the urethra have been made for many years. Marion Douglass, in a paper presented before the American Gynecological Society in May, 1931 reviews some of the historical aspects of this subject. In 1849, Lamballe discussed the causes and treatment of defects of the urethra. Baker Brown in 1863, made a urethra by producing a punctured wound with a trocar below the clitoris

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\*Read at a meeting of the Obstetrical Society of Philadelphia, December 3, 1931.

into the bladder. Into this opening he placed a silver catheter and eventually, after healing, the patient was continent. This was the first reported cure. Lawson Tait in 1878, made the first autoplasmic repair of defects of the urethra and was followed by Schroeder, Freund and Pozzi. Kelley tunnelled the anterior vaginal wall in front of the fistula and transplanted a flap of vaginal mucous membrane, taken posterior to the opening, into the tunnelled tract.

In many of these early attempts, the operation was successful in constructing a new passage for the urine and in closing the fistula but the patient was still incontinent. What little success obtained was due to lengthening the tube and having its outlet at a higher level than normal. There was no sphincteric control. In 1918, Taussig did a unilateral transplant of some fibers of the levator ani muscle with a result so satisfactory that, it stood the strain of a subsequent pregnancy without loss of bladder function. Since then various operations have been proposed to utilize transplants from the levator ani and other muscles to obtain sphincter action.

Marion Douglass has recently reported three successful cases. In his operation, he uses a transplanted flat flap of vaginal mucous membrane with transplants from levator ani muscles to encircle the new tube. These cases have been followed for periods of from four to six years and except for the occasional escape of a few drops of urine, are entirely continent.

Dr. Fred J. Taussig, in a personal communication, writes as follows:

"I have had probably, all in all, about six cases in which there was a complete absence of the urethra and an attempt made to build up a new sphincter. Two of these resulted from an extensive laceration following childbirth and four followed primary carcinoma of the urethra with resection of the urethra and an attempt to build up a new urethra subsequent to this excision.

"I should say that none of my results have been more than partially successful. The best were obtained in cases of primary carcinoma of the urethra where a rim of bladder detrusor muscle with some little remnant of internal sphincter could be utilized at the time of the primary operation in the reconstruction of the urethra. Where a considerable time has elapsed and the sphincter has atrophied, results are very discouraging. Some fifteen or twenty years ago, I operated upon a case that had previously been operated upon by Price in Philadelphia and Kelly in Baltimore without success, and, I had what I would call an 80 per cent successful result. In this case, I took a flap of muscle from the levator on each side, swung it forward underneath the urethra and fastened it there to either side of the reconstructed canal. By a strange coincidence, Dr. H. S. Crossen, this very morning, operated on a similar case and employed the technique which I described at that time. I, also, in one operation where there was a rupture of the symphysis as well as complete rupture of the urethra at delivery, employed the technique of dissecting a strip of rectus fascia and pyramidalis muscle from either side and swinging it down under the urethra so as to exert an uplift pressure. In my case it was a failure. I am so pessimistic as to the possibilities of building up a new urethra satisfactorily, that in every case of carcinoma of the urethra in the past ten years, I have refrained from complete surgical excision but instead have used radium or gold radon seeds. The trouble with these urethras is not any difficulty in making a canal but in getting a sphincter that will function. In most of cases, there is a partial dribbling through the nozzle when the tea kettle fills up."

In ten years, 1910-1918, four cases of total destruction of the urethra were admitted for repair, to the Women's Hospital, New York. Reginald M. Rawls, operated upon three of these cases. In one case, he used the technic suggested by Taussig and after ten operations, succeeded in restoring the urethra and closing the fistula. In his second case, he restored two thirds of the urethra by suturing vaginal flaps over a catheter without attempting to transplant the levators. In his third case, he used the technic suggested by Ward in 1923, as modified by the suggestion offered by Farrar. This case was continent for forty-six months when she reported urgency and slight incontinence under emotional stress or any unusual exertion.

Carey Culbertson operated on one case in 1928. He used the technic of Dudley with an unsatisfactory result. The second operation after the Taussig technic was partly successful for continence. A third operation after the method of Douglass and McGraw was successful and when last seen in November, 1930, was still continent.

N. Sproat Heaney has recently operated upon a case by the Ward technic but the results have not been entirely satisfactory and the operation has been too recent to evaluate the final results.

I am informed that George Gellhorn and Reuben Peterson have recently operated upon cases of this type but their operations and results have not been published.

In the past three and one-half years, there have been published seventeen articles on reconstruction of the female urethra. This would indicate that, while the condition is a relatively uncommon one, the subject is receiving considerable study by gynecologic surgeons.

A careful reading of the literature indicates that various types of operation will succeed in restoring the urethra and in closing the fistula but fail in restoring continence. The late Dr. Polak, stressed the number of failures, even in the hands of expert plastic surgeons, and called attention to the brilliant results obtained in colon implantations of the ureters by the Coffey technic.

In 1923, George Gray Ward, reported a successful result in a case of large vesicovaginal fistula complicated by the absence of the urethra. The first operations were designed to reduce the size of the fistulous opening and restore the urethra by uniting flaps over a catheter. The operations were successful in reducing the size of the opening but failed in restoring the urethra and sphincteric control. He finally operated successfully, using the Kelly method and reinforcing the base of the bladder by a transplant from the labia minora, as suggested by Noble.

In the discussion Lillian Farrar made a valuable suggestion to improve the operation. She suggested that the vaginal flap be made wider so that the lateral edges could be united to form a tube and the tube, instead of a tongue of tissue, made to form the new urethra.

In a recent communication, Ward informs me that he has not had an opportunity to do the operation as suggested by Farrar. The operation has been performed by Guthrie and Haines, with failure; by Rawls successfully; by N. Sproat Heaney with partial success and successfully by me in two cases.

In my cases, I varied the technic as originally proposed by Ward and Farrar. In making the tube graft, the incision is started at the level of the anterior margin of the fistula, instead of the posterior margin. A flap, one inch in width, will form a tube approximately one third of an inch in diameter and with normal contraction of tissue, will form a tube, not more than one fourth of an inch in diameter. A narrower flap will form a tube of too small a caliber. Two fine catgut sutures on either side attach the pedicle of the tube to the posterior rim of the vaginal puncture, just in front of the fistula. A plain rubber catheter is now passed through the tube into the bladder so that five or six inches of the catheter is in the bladder. A traction suture is passed through the proximal end of the catheter and the excess of the catheter beyond the traction suture cut away. The tube with the inserted catheter is drawn through the tunnel and the edges of the tube sutured to the edges of the puncture wound, just beneath the clitoris. The anterior rim of the posterior puncture hole is now sutured to the posterior surface of the tube. The tube is thus anchored throughout its entire circumference to both the anterior and posterior puncture wounds of the tunnel, thus preventing leakage of urine to the operative field. The high point of starting the deundation for the formation of the tongued tube permits the encircling of the tube at the vesical end by a constricting band of tissue, after the method of Kelly. This is a most important step in the operation as it tends, as in my cases, to promote continence. The area of deundation in the vaginal wall is closed by interrupted sutures of catgut or in the exceptional case, by the method of transplants, as was done in Ward's case. The catheter is now partly withdrawn about four inches and fixed so that it cannot fall out of the bladder. The catheter remains *in situ* for eight to ten days. Taussig suggested suprapubic drainage but with a retention catheter functioning, I cannot see the need of this procedure.

I found this operation to be a very simple one, easily and rapidly performed. On account of its simplicity, ease of performance and promise of a successful issue, I believe it to be the operation of choice in this type of case. If the tube remains intact but continence is not gained, it can be supplemented at a later operation by surrounding the tube at the vesical neck by implants from the levator as suggested by Taussig and Douglass. The tongued tube graft is certainly superior to the flat flap of mucous membrane either drawn through a tunnel or sewed to the anterior vaginal wall and reinforced and covered with lateral vaginal flaps.

Undoubtedly, many cases will fail to give satisfactory results no matter what method or methods may be used. In these cases, we still have rectal implantation of the ureters by the Coffey technic. The Coffey method is a great contribution to ureteral surgery and when properly carried out, has yielded satisfactory results. The operation, however, is at times, exceedingly difficult and is not devoid of operative risk and postoperative morbidity and mortality. I am convinced that it should not be done in these cases until plastic repairs have been exhausted.

I have seen three cases of vesicovaginal fistula associated with complete absence of the urethra.

CASE 1.—First seen in 1925, in Sayre, Pennsylvania at the Robert Packer Hospital. The patient had a difficult instrumental delivery in 1919 which was followed by a vesicovaginal fistula. From 1919 to 1922, when she entered the Packer Hos-



pital, she had been operated upon unsuccessfully twelve times in one of the larger cities. During the next three years, three attempts were made to close the fistula and reconstruct the urethra which resulted in failure. When I saw her, she had a fistulae about three-eighths of an inch in diameter and a complete absence of the urethra. I suggested the operation perfected by Ward and Farrar and with the aid of a few rough sketches and models of cut paper, made the technic of the operation understandable. She was operated upon by this technic, this making the sixteenth operation tried. Dr. Haines writes me "apparently there was a perfect result for several days following the Ward operation." Owing to several (15) former operations, with resulting scar tissue, there apparently was not sufficient blood supply to nourish the flap which necrosed. Subsequent to this failure, Doctors Guthrie and Haines transplanted the ureters into the colon and reported the successful result before the Medical Society of the State of Pennsylvania, October, 1926. Five years later, in 1931, other than a mild colitis at times, she is in excellent health and has no difficulty in bowel control of the urine.

CASE 2.—Married, white, aged twenty-eight. One child after normal labor, eight years ago. Incontinence of urine for the past two years. Examination discloses a vesicovaginal fistula, three-eighths of an inch in diameter at the site of the vesico-urethral juncture. Except for the external urinary meatus, there is an entire absence of the urethra. We were unable to obtain from her history any facts which would point to the etiologic factors for the defects. No previous attempts had been made to close the fistula or reconstruct the urethra. She was operated upon eleven months ago by a modified Ward-Farrar method and when seen two weeks ago, was dry and continent.

CASE 3.—Virgin, white, with subnormal mentality, seventeen years of age. She had been under institutional care for some years and so far as we could learn, had always been incontinent. One attempt had been made to close the defect by the plastic flap method with failure. Examination revealed a vesicovaginal fistula, one-fourth of an inch in diameter and a complete absence of the urethra. Operation was not considered at this time. The difficulties of curing the defects by a plastic operation seemed insurmountable and the only procedure which gave any hope of a successful issue seemed to be transplantation of the ureters. I did not feel that I had the moral right to attempt such an operation in this case. The patient, on account of her age and subnormal mental state, was not qualified to assent to the operation, and we were unable to locate her parents or any near relatives.

I saw this patient a year later, after I had successfully operated upon the other patient. I now felt justified in attempting the same operation. The operation was done eleven months ago, by the same technic except that I had to make a wide lateral incision in the vagina in order to obtain sufficient exposure of the operative field. At the present, the result is satisfactory except that there is a dribbling if she allows the bladder to become overdistended. If she voids every six hours, she is both dry and continent.

While this case does not represent a complete and satisfactory cure, nevertheless, her condition at the present time is a marked improvement over her original condition. She is no longer a burden to the institution and is able to do the tasks assigned her.\*

1900 RITTENHOUSE SQUARE.

(For discussion, see page 292.)

\*Since reporting the above cases, case No. 3 returned to the hospital on December 3, 1931. In January of the present year, I reoperated. Examination disclosed the new urethra to be intact, but she had no sphincteric control.

In January of the present year, I transplanted a flap of the recti muscle with fascia attached, carrying the flap behind the symphysis and then splitting the muscles to encircle the urethra.

Up to the present date, the operation has been successful, inasmuch as she has full control of the bladder.

# PRIMARY CARCINOMA OF THE OVIDUCT, WITH A REPORT OF TWO CASES\*

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THESE two cases of primary carcinoma of the oviduct are of unusual interest, first, because of the comparative rarity of the disease, and second, because in the first patient the uterus was not involved, while in the second patient the uterus was involved with tubal carcinoma.

CASE 1.—Mrs. C. B., colored, fifty-three years of age, married, was admitted to the Gynecological Service of The Brooklyn Hospital on October 11, 1931, complaining of severe, cramplike pains in the lower abdomen. The patient had been suffering for three months with cramplike pains in the lower abdomen and frequent micturition. A feeling of pressure on bladder and rectum had been growing constantly worse.



Fig. 1.—Case 1. Right tube an irregularly shaped mass 10 by 6 cm. in diameter, the left a sausage-shaped mass 12 by 5 cm. The mass in the center is the uterine body containing several small myomas.

For the last month constipation had been a troublesome factor. For the past year the patient had noticed a thin watery, bloody, foul vaginal discharge.

The menstrual history was that her periods had always been regular up to the time of her menopause, four years ago. Since then, there had been no vaginal flow until one year ago. The patient admitted three labors and two miscarriages, and the last pregnancy was twenty-three years ago. The urine was negative. Hemoglobin 93 per cent, R.B.C. 4,560,000, W.B.C. 11040, polymorphonuclears 69 per cent, sedimentation time thirty minutes.

On examination, the patient was large, stout, and had good color. There was no suggestion of cachexia, and she did not appear ill. Abdominal examination revealed a fixed, hard mass extending from the pelvis nearly to the umbilicus. The mass was irregular, and only slightly tender. Vaginal examination showed a multiparous introitus from which a thin bloody discharge was draining. The cervix was normal in size, and slightly eroded. It was fixed solidly into the hard, irregular, fixed pelvic mass. In the posterior culdesac there was a more elastic mass which pressed on the

\*Read at a meeting of the New York Obstetrical Society, December 8, 1931.



Fig. 2.—Case 1. Section showing tube wall at the bottom and papillary growth in the lumen with thin mucus between the projections of the tumor.



Fig. 3.—Case 1. Higher power showing details of the papillary structures and the resemblance to folds of oviduct mucosa.



Fig. 4.—Case 2. Low power showing part of tube wall at the bottom and papillary projections of the tumor growing into the lumen.

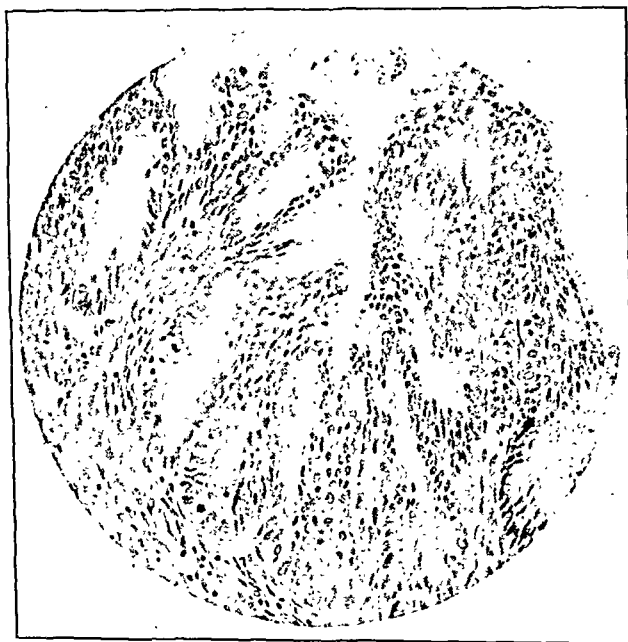


Fig. 5.—Case 2. Papillary formations are coarser than in Case 1. The epithelial cells are smaller and are more similar to those of normal oviduct epithelium.

anterior rectal wall. Rectal examination showed this mass to be the size of a good sized lemon, and that it markedly interfered with the lumen of the rectum.

A diagnosis was made of an old uterine fibroid with malignant degeneration. Exploratory laparotomy was advised with removal of the mass to relieve the pressure symptoms, even though the tumor was probably inoperable.

*Operation.*—Supravaginal hysterectomy with double salpingo-oophorectomy. The abdomen was opened in the midline below the umbilicus. Some free bloody fluid was found in the abdominal cavity. Adhesions were everywhere, old and dense. The mass was found to consist of a normal sized uterus surmounted by a fibroid the size of a small lemon. The remainder of the mass consisted of the right and left fallopian tubes. The ovaries were not identified. The tubes were markedly enlarged, measuring roughly, 4 by 2 inches, and had the appearance of chronic pyosalpinx. The adhesions were freed with difficulty, the uterus and tubes were removed unruptured, vessels ligated, and the abdomen was closed without drainage.

On account of this unusual history and findings, the pathologist was requested to examine the specimen at once. On gross examination of the contents of one tube, he made a probable diagnosis of carcinoma of the oviduct.

*Gross.*—Specimen consisted of a uterus with both tubes. The uterus was small, and had been amputated supravaginally. The upper part of the uterus contained a small myoma. The uterine cavity was small, the mucous membrane was thin, and pale red in color. The ovaries were not recognizable in the material. The right tube was a potato-like mass about 10 cm. long, and 7 cm. in diameter. Externally it was smooth. On section, the wall was about 4 mm. thick, and the cavity was filled with gray, softened tumor material. The left tube was sausage shaped, 12 cm. long, and 5 cm. in diameter. It was smooth externally. The wall was thin, and the cavity was filled with coagulated mucus. Growing from the internal surface were numerous warty, white outgrowths of tumor.

*Histologic.*—Sections showed a papillary mucus secreting tumor, which formed structures more or less like the folds of oviduct mucosa. In neither tube did it show a tendency to penetrate the muscular wall of the oviduct. The uterine endometrium showed no carcinoma.

*Diagnosis.*—Primary carcinoma of oviduct, bilateral.

The patient had a fairly smooth convalescence, and the wound healed by primary union.

We have one other case of primary carcinoma of the oviduct in the records of The Brooklyn Hospital.

CASE 2.—The history of this second case is as follows:

Miss E. H. was admitted to the Gynecological Service on October 7, 1924, with a diagnosis of adenocarcinoma of the uterine body. The pathologist confirmed the diagnosis from curettings, and 2400 mg. hours of radium were given. The patient was readmitted six weeks later and a complete hysterectomy and bilateral salpingo-oophorectomy were performed for adenocarcinoma of the corpus uteri. The pathologic diagnosis was primary bilateral adenocarcinoma of fallopian tubes, with extension of tubal carcinoma into the corpus uteri. Grossly, the tubes were not very large. Under the microscope the new growth in the uterine cavity very closely resembled tube epithelium.

The patient was again admitted on January 28, 1926, with a recurrence of carcinoma in the vault of the vagina. One thousand two hundred mg. hours of radium were given. The patient was in poor general condition, and probably died in Ireland during the following year.

# OBSERVATIONS ON THE (CYCLICAL) PELVIC FLUID IN THE FEMALE\*

## A PRELIMINARY REPORT

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MY PURPOSE in announcing the results, though incomplete, of a study which I am now making of the peritoneal fluid found in the pelvic cavity during the menstrual cycle, is simply to place on record a brief statement of some interesting findings made by me during the past fifteen years. Until recently I believed these observations commonly accepted by gynecologists. However, I find that they are not and also, that little has been written on this subject.<sup>1</sup> I began several months ago, with the kind cooperation of my colleagues at the Woman's Hospital, a systematic study of what I here term the cyclical pelvic fluid in the female. These observations point to the following conclusions: In the pelvic cavity of every woman with normally functioning ovaries, there is a fluid of a definite character, color and quantity. Under normal conditions this fluid is found collected in the culdesac, but, if a large fibroid of the uterus exists, some of it will be found anterior to the uterus and broad ligaments. In cases of third degree retroversion some of the fluid will be found above the displaced organ.

Its general appearance depends upon its cellular contents and the consistency seems to vary with the stages of ovarian activity. Its essential color may vary from pale green to light yellow or deep amber. The amount of fluid varies in every individual and in every stage of ovarian activity. In this series of cases the smallest measurable amount (half a drachm) was found between the last day of menstruation and the rupture of the graafian follicle; the greatest (2 ounces) between ovulation and the full development of the corpus luteum. The amount present during menstruation has not been noted by me,<sup>2</sup> as no operation was performed during the menstrual period.†

Varied pathologic conditions, such as simple fibroids and ovarian tumors, may be present, without an essential change resulting in the character of the fluid. Acute inflammations, papillary growths, etc., will, however, alter its consistency, color and volume, until the fluid is no longer recognizable.

The fact that no measureable amount of peritoneal fluid of any character is found in the pelvis of woman when the ovaries are not functioning, unless there exists a papilloma or some acute intraabdominal lesion, but is found in varied and measureable quantities during the stages of

\*Read at a meeting of the New York Obstetrical Society, December 8, 1931.

†There were operations performed during uterine bleeding, but, as these patients flowed so irregularly (as the result of fibroid tumors or other pathologies), it was impossible to determine whether these flows were menstrual or not.

ovarian activity suggests that ovarian activity is responsible for the presence of the fluid.

The fact that the greatest amounts of the fluid have been found after the rupture of the graafian follicle, or between its rupture and the full bloom of the corpus luteum, suggests that the presence of the freed liquor folliculi in the pelvic cavity may act as a stimulus to the pelvic peritoneum; also, that the great activity during the development of the corpus luteum may play an important part in the increase of the fluid.

The cyclical pelvic fluid in the female is a physiologic fluid, and serves the definite purpose of transporting the ovum and extending the folds of the fimbriae to their full capacity, at the same time allowing them freedom of motion. Thus spread out in the form of tentacles, they reach well into the pelvic cavity and it is difficult for the ovum to escape. In cases where abnormal conditions of the adnexa exist, such, for example, as an ovary on one side of the pelvis from which the corresponding tube has been removed, and on the other side no ovary and a tube resected, but patent, and nevertheless pregnancy occurs, there can be no explanation more rational than that of the mechanical conveyance of the ovum from one side of the pelvis to the resected tube on the opposite side, by the fluid. As the ovum has no power of motion it must depend upon external force for its migration, and this can be no other than wave motion in the peritoneal fluid, caused by intestinal activity or muscle action of the abdominal walls, through breathing, etc.

As the ovary is the only pelvic organ in the female which is not covered with peritoneum, and as, throughout the entire menstrual cycle, fluid is found in the culdesac, it is reasonable to assume that another of the functions of this fluid is to protect the ovaries during their active functioning.

These conclusions are based upon a study of 37 unselected abdominal sections, in which cases were found such conditions as the following: simple retroversions, retroversions with complications, fibroid tumors of the uterus (with and without the previous application of radium), simple ovarian tumors, malignant papilloma of the ovaries, early pregnancy, chronic appendicitis, pelvic metastases occurring after carcinoma of the cervix had been treated by the application of radium, intrauterine polyp at time of menopause, and congenital ovarian deficiency with infantile uterus.

Studies are being made of the cellular contents of the fluid during the varied stages of ovarian activity, and it is hoped that the ovum will be found in it. This, however, can be expected during only a limited period after the rupture of the graafian follicle. The female sex hormone has not yet been demonstrated in the fluid. Experiments are being made with this in view. Observations are becoming more accurate with experience, and it is hoped that findings will be clarified with further study and analysis.

## TECHNIC

In order to secure the fluid found in the culdesac, unmixed with blood from the abdominal wound, or elsewhere, great care is necessary. On incising the abdomen, each bleeding vessel must be ligated and oozing of blood stopped by hot gauze pads and pressure. When the peritoneal cavity is opened great care must be taken to prevent trickling of blood along the peritoneal wall. The patient is placed in a modified Trendelenburg position and the small intestines are lifted, with the hand, out of the true pelvis, and held above the brim of the pelvis by means of rubber envelop pads. The fluid is then withdrawn with an Asepto syringe, to the end of which is attached a short, straight, rubber female catheter. Care should be taken to avoid the catheter coming in contact with the wound, as any contact with the bleeding surface would necessarily convey blood to the fluid. If the uterus is in a normal position it should be forced slightly forward, by means of a trowel retractor, never by a vulsellum forceps, nor by any instrument which would occasion bleeding. If it is retroposed, the fluid situated above the corpus should first be withdrawn. The corpus should then be placed, manually, in an extreme anterior position, after which the remaining fluid in the culdesac may be withdrawn. During this process no gauze pads nor probangs should be used, as the fluid would be unavoidably absorbed thereby.

## REFERENCES

- (1) *Novak, J.*: Zentralbl. f. Gynäk. 46: 854, 1922. (2) *Frank*: Gynecological and Obstetrical Pathology, p. 428.

219 WEST SEVENTY-NINTH STREET.

## THE FREQUENCY AND CAUSES OF PREMATURE BIRTH

## A REPORT OF 238 CASES

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THE causal relationship between premature birth and neonatal morbidity and mortality is well known. In many cases the reason for the shortening of the period of gestation is apparent, being preventable in some cases and not so in others. However, in not a few instances no cause can be found to account for the early loss of the products of conception.

The present report concerns the incidence of premature birth, but more particularly the frequency of cases in which no cause for the condition can be found. Records of a consecutive series of 238 immature infants and their mothers form the basis for the report.

An entirely satisfactory definition for prematurity is difficult to make. For the purpose of this study birth weight has been selected as the best criterion. A premature infant is considered to be one which weighs between 1500 and 2500 grams at birth. With this single criterion as a basis, the 238 records previously mentioned were selected.



In a study of 10,000 births, Zweifel<sup>1</sup> found that 965 (9.65 per cent) took place prematurely. His index of prematurity was also body weight; those labors were considered to be premature in onset, which resulted in births of infants weighing between 1,000 and 2,500 grams.

Feldman<sup>2</sup> gives 10 per cent as the frequency of premature births. This percentage is based upon statistics from the Moscow Foundling Hospital (5 per cent), the Clinic Tarnier (10.7 per cent), and from ones given by Pinard (15.4 per cent).

Many causes have been recorded. Hess, Chamberlain, and Lundeen<sup>3</sup> and Zeltner<sup>4</sup> together give reasons for a total of 404 such births. Twinning was found by them to be the most common cause, being responsible for approximately 55 per cent of the known causes. This was followed in order of frequency by toxemia (14.1 per cent), syphilis (7.6 per cent), cesarean operations and induced labors (a total of 3.7 per cent), heart disease (2.9 per cent), pulmonary tuberculosis (2.7 per cent), and nephritis (2.5 per cent). Less frequent causes included: placenta previa, operations in the presence of acute infections, trauma, toxic goiter, asthma, diabetes, epilepsy, pernicious anemia, pyelitis, encephalitis, acute yellow atrophy, shock, and pneumonia.

In a relatively large proportion of instances these authors found no satisfactory explanation for the prematurity. Zeltner<sup>4</sup> learned the cause in only 75 (31.2 per cent) of a group of 240 cases. Hess, Chamberlain and Lundeen<sup>3</sup> located it in only 307 (40 per cent) of 761 cases. It is evident from these figures that the cause of prematurity requires further study.

The 238 premature infants forming the basis for the present study represented 8.2 per cent of 2876 consecutive live births taking place during the period studied. This frequency is practically identical with that of others.

Of the 238 premature labors 47 (19.7 per cent) were induced and 191 (80.3 per cent) were spontaneous. The latter are the ones of chief interest in this study.

The maternal and infant records were searched for the possible causes

TABLE I

		NUMBER	PER CENT
Premature births of known cause		111	100.0
Diseases of uterus, contents, and appendages		73	65.8
Toxemia	28		
Twins	15		
Abruptio placentae	12		
Placenta previa	7		
Stillbirth	4		
Myoma uteri	2		
Premature rupture of membranes	1		
Pain from old suspension scar	1		
Ovarian cyst	1		
Placental infarct	1		
Hydorrhea gravidarum	1		
Syphilis (positive Wassermann test)		21	18.9
Other conditions		17	15.3
Spinal and pelvic deformities	7		
Cardiorenal disease	4		
Pyelitis and cystitis	3		
Neurosis	1		
Imbecile mother	1		
Maternal pulmonary tuberculosis	1		

of the 191 spontaneous births, and as a result possible causes for 111 (58.1 per cent) were established (Table I). If these were not the true causes, they were associated conditions, and the only ones which were found to have any possible bearing upon the cause of the prematurity.

In 80 (41.9 per cent) of the 191 spontaneous premature labors no cause for the condition could be found. It would seem therefore, that approximately 42 per cent of spontaneous premature births, as they are observed in maternity hospitals pass without being satisfactorily explained. This figure indicates the size of the problem of prematurity of unknown cause as it exists today.

The relationship between maternal color and in the incidence of premature birth of unknown cause is shown in Table II. Apparently the condition is equally common in white and black women.

TABLE II

	ALL LIVE BIRTHS	PREMATURE BIRTHS	PER CENT
White patients	1823	50	2.7
Colored patients	1053	30	2.8

In Table III the ages of the women giving birth prematurely to infants, where the cause of the prematurity was not evident, are compared with the ages of an equal number whose infants at birth weighed 3,000 grams or more. The chief point of interest in this table is the fact that so many of the immature infants were born of mothers who were under twenty years of age.

TABLE III

MATERNAL AGE	INFANTS 1500-2500 GM.	INFANTS 3,000 GM.
14-19 years inclusive	22	9
20-24 years inclusive	22	26
25-29 years inclusive	16	21
30-34 years inclusive	12	13
35-39 years inclusive	7	9
40-44 years inclusive	1	1
45-49 years inclusive	0	1
Total	80	80

TABLE IV

	NUMBER OF PATIENTS	PER CENT
Previous pregnancies	44	100.0
Previous pregnancies, normal duration	32	72.6
Short term pregnancies	12	27.4
Miscarriages	4	
Premature births	8	(18.2)
Patient 1, 6 pregnancies, 6 premature; Patient 2, 6 pregnancies, 1 premature;		
Patient 3, 6 pregnancies, 1 premature; Patient 4, 2 pregnancies, 2 premature;		
Patient 5, 2 pregnancies, 2 premature; Patient 6, 2 pregnancies, 1 premature;		
Patient 7, 2 pregnancies, 1 premature, and Patient 8, 1 pregnancy, 1 premature.		

Of the 238 women who had premature births, 44 (Table IV) had had previous pregnancies. Only 8 of these had had previous premature labors. The number of their pregnancies and the incidence of prematurity among them is also recorded.

No information is available concerning the causes of the earlier premature births of the 44 women. However, a fact of interest is that the incidence of *previous* premature births was more than twice (18.2 per cent) that of the ones under investigation (8.2 per cent).

#### SUMMARY

1. Of 2876 consecutive labors in two teaching hospitals, 238, or more than 8 per cent, were premature in onset, as measured by infant birth weight.

2. Approximately 80 per cent of the 238 premature births were spontaneous in onset, the remaining 20 per cent being induced by either medical or surgical means.

3. Of all spontaneous premature labors, the cause of 58 per cent could be determined. Disease or abnormality of the uterus, its contents or appendages was responsible for 73 per cent of known causes.

4. No cause for prematurity could be found in approximately 42 per cent of spontaneous births.

5. Spontaneous premature births of unknown cause were equally frequent in colored and white women.

6. Women under nineteen years of age give birth more frequently to premature infants, than do those in later years.

7. The incidence of premature births appears to be greater in women who have been previously delivered prematurely, than in the population at large.

The authors are indebted to Drs. Edmund B. Piper and Norris W. Vaux for the privilege of examining the records of the University Maternity and the Philadelphia Lying-In Hospital.

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- (1) Zweifel, E.: Arch. f. Gynäk. 101: 643-699, 1914. (2) Feldman, W. M.: The Principles of Antenatal and Postnatal Child Hygiene, London, 1927, John Ball & Sons. (3) Hess, J. H., Chamberlain, I. McKy., and Lundeen, E. C.: Pennsylvania M. J. 33: 429-442, 1930. (4) Zeltner, E.: Gesundheitsförs. f. d. Kindesalt. 4: 493-516, 1929.

## THE USE OF EXTERNAL CEPHALIC VERSION IN AN OUTDOOR MATERNITY CLINIC\*

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ALTHOUGH Wigand described this operation in 1807, it did not acquire a place among the obstetric operations until the beginning of this century and is infrequently used even at the present time.

At the Berwind Maternity Clinic, version was attempted 70 times upon 64 patients without the use of anesthesia. Eighty-seven per cent were successful (Table I). The majority were converted between the

TABLE I

	NUMBER OF CASES	ATTEMPTED VERSION	VERSION SUCCESSFUL	PER CENT SUCCESSFUL
Nulliparae	10	11	9	81
Primiparae	16	17	15	88
Multiparae	38	42	37	88
Total	64	70	61	87

thirtieth and thirty-sixth week, the earliest at the twenty-fourth week. We advise that it be done as early as the twenty-eighth week, for this allows ample time for further attempt if unsuccessful and should the breech recur the version can be repeated, several times if necessary, before the onset of labor. Ryder mentions a case in which the fetus was turned four times. An external version was finally done in the first stage of labor under anesthesia, and the membranes ruptured to maintain the cephalic presentation. The patient had a normal delivery.

It seems to make little difference whether the baby is turned clockwise or counter clockwise, although we prefer turning the head towards the fetal small parts, but if an attempt in one direction fails we turn it in the opposite direction.

In 9 patients the version was unsuccessful. Four were in the last month of gestation and delivered as breech. Of the remaining 5, which were attempted before the thirty-fourth week, 4 delivered as vertex.

The difficulty of performing this operation is very much exaggerated. The resident staff and students have done the operation without difficulty. Occasionally a case is encountered which cannot be turned.

At times the breech recurs spontaneously after successful version, but can easily be reconverted. In 2 patients the version was performed twice and one three times before the presentation remained vertex.

\*Read in part at the Section of Obstetrics and Gynecology at the New York Academy of Medicine, April 28, 1931.

Two cases successfully converted recurred spontaneously and delivered as breech, one of which had been turned twice. The frequency of spontaneous version decreases rapidly as full term is approached and seldom occurs in the tenth month.

Although practically all of the earlier writers advised that some sort of support, pillow, or bandage be applied to retain the fetus in its new position, we did not use any binder after successful version, as it was found that the proportion of recurrence is fully as great with as without bandages.

We do not use the Trendelenberg position nor the knee-chest posture to disengage the breech prior to version. The patient is placed on a flat table with knees drawn up and head raised to allow relaxation of the abdominal muscles, the bladder being empty. The breech of the baby is grasped, pushed upward out of the pelvis and to one side. Although some operators spend the great part of their effort in turning this pole, we direct most of our attention to moving the head down toward the pelvic inlet.

The age of these patients varied from eighteen to forty-four. The average parity was 2.6. Two were para xii, and in 3 cases the parity was not stated. In 11 the position was transverse and the remaining 53 were breech deliveries. In some cases after successful version, the head was not felt in the lower uterine segment by abdominal palpation but was readily determined by a vaginal examination. X-ray examination has been suggested as a further means of corroborating the position both before and after version.

We cannot agree with Miller that breech cases are fraught with little or no danger. The average fetal death rate in vertex presentation is 2 to 4 per cent. Meyer lists 20 authors reporting a mortality in breech deliveries between 10 to 40 per cent. Others (Polak, Golabin, Kraus, Pierson, Dubois, etc.) have found a death rate in primary breech deliveries from 10 to 37 per cent. In 4488 patients at Berwind Maternity Clinic there were 164 primary breech deliveries, with a gross fetal mortality of 12 per cent. A mortality of 10 to 15 per cent in primary breech deliveries is considered conservative. Add to this that in breech cases the mother runs more risk of deep tears, postpartum hemorrhage, and infection.

The average duration of labor was thirteen hours, the shortest was four hours, and the longest twenty-eight hours due to a large baby, weighing 11 pounds. The pelvis was generally contracted in 8 patients, absolute contraction in 1, simple flat in 3, funnel in 2, and rachitic in 3.

Contracted pelvis has been advocated as a contraindication for external version (Southwick, Martin, et al.), on the theory that the after-coming head is more easily delivered and that the breech presentation obviates the necessity for internal version. Internal podalic version and

extraction, however, is no longer the accepted operation in contracted pelvis. A trial of labor, followed by cesarean section if the head fails to engage, is now considered the better procedure. A great many patients with relatively contracted pelvis deliver spontaneously or with forceps after a trial of labor if the baby presents by the head, but might be subjected to cesarean section if the presentation were breech. It would, therefore, be especially desirable in relatively contracted pelvis, to convert a breech to a cephalic presentation to allow of trial labor. Only in an absolute pelvic contraction is an external version not necessary as an elective section is indicated.

There was no fetal mortality in our series. Possible complications such as premature separation of the placenta, prolapse of the cord, rupture of the membranes, etc., were not encountered. There were two premature births which could not be attributed to the external version.

#### SUMMARY AND CONCLUSIONS

In 64 patients external cephalic version was successfully done in 87 per cent without the use of anesthesia. There was no fetal mortality, and no complications were encountered. The operation should be done as early as the twenty-eighth week to allow for repetition if the breech recurs, or it can be attempted at successive visits if unsuccessful at first. The baby can be turned in either direction and abdominal supports are unnecessary. The mortality of the fetus in breech deliveries is definitely greater (10 to 15 per cent) than in vertex presentations (2 to 4 per cent), but we have at our disposal a safe and comparatively simple operation of converting breech and transverse presentation to vertex by means of external manipulations. In relatively contracted pelvis trial labor can be allowed with a vertex presentation, but would not if the presentation were breech, thereby reducing the incidence of operation.

55 EAST EIGHTY-SIXTH STREET.

## REPORT OF A CASE OF (UTEROPLACENTAL) APOPLEXY IN ACCIDENTAL HEMORRHAGE

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THE patient, aged twenty-five years, para ii, was first seen by one of us on May 28, 1931, at 6:30 P.M. at her home. She stated that at 1:00 P.M. she developed acute pain in the back extending to the right side of the abdomen. Later it became localized in the right iliac region, and was continuous and severe. Vaginal bleeding, dark in color in the beginning, later bright red, began suddenly with the onset of pain, and continued throughout the afternoon. She believes she used about fifteen napkins. Nausea was present, but patient did not vomit. There were momentary periods of dizziness, especially if she attempted to sit up or walk.

She attributed her condition to a nervous shock the day before. She was very nervous the remainder of the day and went to bed with a severe headache. A month before she had had a similar attack of lesser degree, following an accident in which her foot was caught in the step of a bus, twisting her body and causing her to fall to the ground. She was advised by her physician to remain in bed and apply an icebag, but he did not visit her. There was no bleeding at this time.

Her last period occurred on November 1, 1930. Nausea and vomiting were present during the second month. She had suffered from fleeting headaches, dizziness, and extreme nervousness, usually around the times of her expected periods. She does not know whether her blood pressure was high during this pregnancy, and if there was any albumin in her urine she was not so advised. She had been under treatment for the past two years for uterine displacement and "inflammation of the tubes." She had a tonsillectomy in September, 1930. She had a dead, abscessed right upper molar which had been tender for years.

Five years previously her first pregnancy was terminated by a difficult forceps operation after a long labor at term. Hypertension and albuminuria were present. The child is living and well. No history of abortions.

Her family and past personal history offer nothing of importance.

Examination: Pulse, 72; temperature 98.6° F.; respirations 20; blood pressure 140/80. She appeared to be suffering severe pain and was vainly attempting to find a position which would secure relief. Although of a florid coloring, there was a slightly ashen color in her face. The heart and lungs were negative. The abdomen was enlarged, and the uterus tetanic and of ligneous consistency. It extended to four fingers above the umbilicus. No fetal parts could be felt over any part of the uterus; marked tenderness was noted over the whole abdomen, especially over the right iliac region. No fetal heart tones could be heard after repeated examinations. The maternal pulse could be heard distinctly in both iliac regions and above the pubis. There were no uterine contractions.

Rectal examination showed about 1 cm. dilatation, no effacement, and the head felt low down. Nothing suggestive of a placenta previa could be felt.

She was sent to the Hollywood Hospital after an injection of morphine sulphate, gr.  $\frac{1}{4}$ , and atropine sulphate, gr. 1/150, which gave her considerable relief. A blood count taken at 8:00 P.M. showed hemoglobin 62 per cent; R.B.C. 3,160,000; W.B.C. 14,000; polymorphonuclears 88 per cent; lymphocytes 11 per cent; transitionals 1 per cent. Coagulation time four and a half minutes. A catheterized specimen of urine, sp. gr. 1.028, revealed two plus albumin and few granular casts and white blood cells.

Another red cell and hemoglobin count was taken at 10 P.M. after  $\frac{1}{3}$  grain of pantopon had been given hypodermically. The hemoglobin was 57 per cent; erythrocytes, 2,730,000. The pulse was 90. No fetal heart tones were heard and there were no uterine contractions. There was moderate vaginal bleeding of a serous nature.

A diagnosis of premature separation of the placenta and fetal death with possibility of uteroplacental apoplexy was made, and in view of the fact that the cervix was undilated, that there were no uterine contractions, and there were evidences of both external and concealed hemorrhage, it was though advisable to interfere while her condition permitted. Laparotomy with hysterotomy, or possible hysterectomy was the operation selected.

Operation was begun at 11:40 P.M. under ethylene-oxygen anesthesia preceded by injection of pantopon gr.  $\frac{1}{3}$ .

With the patient in a moderate Trendelenberg position a median incision from above the umbilicus to the pubis was made and a moderate amount of serosanguinous fluid in the peritoneal cavity was revealed. The uterus was about the size of an eight months' pregnancy, ovoid and extremely hard, especially in the lower uterine segment. There was a widely diffused ecchymotic discoloration over the whole of the surface of the uterus, to a greater degree over the lower uterine segment which was almost black. The subperitoneal hemorrhage extended into the broad and infundibular ligaments. In the right infundibular ligament was a small hematoma. The fetal parts could not be felt. The ovaries were large and of the oyster type. The tubes, except for the ecchymoses, appeared normal. A normal appendix appeared in the field of operation and was not disturbed. On account of the widespread infiltration of the uterine muscle by the hemorrhage it was thought advisable to extirpate the uterus with contents as rapidly as possible.

A supravaginal hysterectomy of the intact uterus, conserving the tubes and ovaries, was performed in forty-five minutes. She was in fair general condition with pulse of 114 and good quality at the end of the operation.

Pathologic report (Dr. V. L. Andrews, pathologist): "Specimen is a uterus, enlarged, containing a male fetus of about seven and a half months. The serosa covering the anterior surface of the uterus is dark colored and the underlying muscle tissue is heavily infiltrated with blood for a distance of 5 mm. Section through the uterine muscle and exposing the fetus and contents, shows a large hemorrhage behind the placenta. The lower uterine segment segment composing the cervical canal is thin and the entire musculature is heavily infiltrated with blood. From the beginning of the internal os upward the infiltration of the musculature is more on the surface of the uterus than in the body of the muscle."

Immediately after operation 1000 c.c. of normal salt solution was given intravenously and alternating every four hours with 5 per cent glucose solution by hypodermoclysis. This was continued for forty-eight hours, followed by fluids by mouth which were well tolerated. Pantopon was given in sufficient amount to control pain and restlessness. On the third day she was placed on a soft diet, and was given liver extract with iron. There was no distention and the bowels moved well with the assistance of small enemas. There was a moderately severe cystitis following catheterization during the first twenty-four hours, and she complained of pain and paresthesia along the ulnar distribution in the left forearm and hand; this together with a hyperirritability and emotional instability was fairly well controlled by intravenous injections of a calcium chloride preparation daily for five or six days. A blood calcium determination on the fifth postoperative day was 7.9 mg. per 100 c.c. The hemoglobin was 41 per cent; R.B.C. 2,100,000. The urine was loaded with pus cells and two plus albumin.

The maximum rise in temperature occurred on the second and the sixth postoperative days when it was 100.4° F.; pulse was 110.



She left the hospital on her fourteenth postoperative day, having had a normal pulse and temperature for one week. Hemoglobin on discharge was 46 per cent; R.B.C. 3,010,000.

After leaving the hospital, she was placed on a liberal diet. Rest, cod liver oil, and continued use of liver extract and iron were prescribed. Vasomotor disturbances were very annoying and were controlled by biweekly injections of ovarian hormone. There was no vaginal discharge at the end of six weeks; the urine was negative. The vaginal stump was freely movable without pain.

On October 15, 1931, her weight was 116 pounds; hemoglobin 65 per cent; R.B.C. 4,200,000. There were no symptoms and she felt better than she had felt for years.

#### COMMENT

In this case, of toxemia, accidental torsion occurring the previous month with a mild reaction, combined later with a nervous shock were undoubtedly etiologic factors in the production of a uteroplacental apoplexy.

1052 WEST SIXTH STREET.

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Wislocki, George B.: Observations on the Placenta from a Case of Malaria. Bull. Johns Hopkins Hosp. 47: 157, 1930.

The study of the placenta from a case of malaria affords proof that the chorionic syncytium is incapable of phagocytizing an inert suspension of pigment present in the intervillous spaces or of transmitting such particles from mother to fetus. Malarial parasites are present in the placenta in great abundance within the erythrocytes in the intervillous spaces. Malaria induces the accumulation of large numbers of monocytes and lymphocytes in the placental circulation. Of these cells, the monocytes phagocytize abundantly pigment released by the activity of the malarial organisms. These phagocytic monocytes do not penetrate the fetal tissues, but do enter the masses of fibrin formed on the villi which are denuded of syncytium at these sites. Typical clasmatoocytes are not encountered in the intervillous spaces. The monocytes and lymphocytes which gather in the placenta are brought there from other parts of the maternal body where they are produced. The villi, including their stroma and covering chorionic syncytium, are anatomically normal and not visibly affected by the malarial organisms or their products. It is unlikely that malarial organisms can enter or penetrate the chorionic syncytium, so that the transmission of malaria from mother to fetus occurs rarely if at all.

C. O. MALAND.

Ronsisvalle: Ovarian Cystoma Complicating a Seven Month Pregnancy Masked by Ascites. Arch. obst. e ginec. 17: 474, 1930.

The author calls attention to diagnostic difficulties sometimes presented by ovarian tumors complicating pregnancy. He reports a case in which the presence of the cystoma was obscured by a large quantity of ascitic fluid in the abdomen.

Cases of this sort are not so rare. Removal of the tumor by laparotomy often permits pregnancy to continue to term.

SYDNEY S. SCHOCHET.

JULIUS E. LACKNER.

# Society Transactions

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## NEW YORK OBSTETRICAL SOCIETY

MEETING OF DECEMBER 8, 1931

DR. WILLIAM S. SMITH presented a report of two cases of **Primary Carcinoma of the Oviduct**. (See page 267.)

### DISCUSSION

DR. G. L. MOENCH.—I have observed only one case of primary tubal carcinoma in six years and that was limited strictly to the tube. Like some of the cases reported in the literature, the wall in this particular case was exceedingly thin, with a polypoid growth inside. The patient was subjected to operation, but she died in about eleven months of a brain metastasis.

DR. IRA I. KAPLAN.—In our service at Bellevue Hospital, during the past eight years we have had referred for radiation therapy only two cases out of several hundred gynecologic patients of carcinoma of the fallopian tube.

CASE 1.—N. W., aged twenty-nine, married. Was operated upon in December, 1926, for vaginal bleeding, following a seven weeks' period of amenorrhea. Operation revealed a carcinoma of one fallopian tube. In May, 1927, she returned to the hospital for recurrent bleeding since March, 1927. She was referred for x-ray therapy and reacted well to the treatment, all bleeding ceasing after treatment. She was seen again in November, 1928, and had had no bleeding and her general condition was good. Recent follow-up by the Social Service shows the patient alive in the summer of 1931, since which time all trace of her has been lost.

CASE 2.—F. D., aged thirty-two, married, referred to Bellevue Hospital for post-operative x-ray therapy. Previous to operation on January 7, 1929, she complained of pain and swelling in the abdomen. Operation revealed a carcinoma of the fallopian tube with metastases to the pelvis. Following irradiation the patient was fairly comfortable until June, 1930, the swelling of the abdomen became more marked and in August, 1930, she was again operated upon but an attempt to remove the tumor masses was unsuccessful. She died October, 1930, from generalized metastases.

In the two cases herewith reported, irradiation following operation did help ameliorate the condition, it prolonged life in one case. I am of the opinion that as in ovarian carcinoma, preoperative irradiation would be of great benefit in limiting the extent of the disease.

DR. DOUGAL BISSELL presented **Observation on the Menstrual Cyclical Pelvic Fluid**. (For original article see page 271.)

DR. LOUIS E. PHANEUF (by invitation) read a paper entitled **Radium Therapy in Uterine Hemorrhages of Benign Origin**. (For original article see page 225.)

### DISCUSSION

DR. GEORGE G. WARD.—I have looked over the records at the Woman's Hospital and found in the past five years 309 cases of the type discussed. Of great

interest in these cases is the treatment by radium of the young girl who bleeds excessively. In my series I had four cases under twenty years of age. One girl, nineteen years old, had been having an excessive flow at each period, with marked anemia as a result, for about two years. Repeated curettages were without avail and, therefore, we subjected her to radiation. She was given 300 mg. hours with satisfactory result, menstruating normally. The second case was seventeen years of age, also had had repeated curettages. She was given 250 mg. hours with a partial result. I might say here that in young girls we use a very small dose of radium with the understanding that we may have to repeat it. If you use as much as 500 or 600 mg. hours, permanent amenorrheas may result. We, therefore, underradiate in young women even though it may be necessary to repeat the dose later on. The third case was twenty years old and she was given 200 mg. hours with satisfactory results. We saw her two years later and her periods were absolutely normal. The fourth case was sixteen years of age. She had been having a profuse flow and had been curetted without result. Three hundred mg. hours were given her with satisfactory result. That patient was seen two years later.

As an example of overirradiation I would like to mention the case of a young lady, twenty-four years of age, prominent socially, who had a similar history. She was given 1440 mg. hours by a well known radiologist, two years ago, and has now a permanent atrophy with amenorrhea. I mention this to show what a very dangerous weapon radium is if it is not used properly.

To show how variable radiation is I would like to mention a case which is rather extraordinary in my experience. The patient, a colored girl, was admitted to the Woman's Hospital May 3, 1925. She was twenty years old and had been married eight months. She gave a history of severe hemorrhages, was suffering from extreme anemia and had been transfused. A dilatation and curettage was done. The pathologic report showed placental tissue. She evidently had been pregnant and miscarried. The pathologist added that there was strong evidence pointing to chorionepithelioma. On May 12 she was given 101 mg. of radium in tandem form for twenty hours. She was again transfused May 12 and May 19. Her hemoglobin was 41 per cent and the red cells were 3,080,000. She was discharged June 5, 1925. We saw her the following month, she was apparently all right and had stopped bleeding. She had no menstruation for five months following radiation, then menstruated regularly, flowing for about two to three days, until May, 1927, when she became pregnant. She had a normal labor in February, 1928, in the Woman's Hospital. The baby weighed 6½ pounds, perfectly healthy and well-formed. Since that time she has been pregnant twice and has miscarried each time. It is extraordinary that after a radiation of 2000 mg. hours and menstruation being stopped for five months that the patient subsequently had a normal child. Her following pregnancy dated from July, 1928. She was readmitted to the hospital October, 1928, with a history of a profuse flow. Examination at this time showed the uterus enlarged to the size of a six weeks' pregnancy. A diagnosis of incomplete abortion was made and she was curetted. Pathologic report showed placental tissue. Her periods then continued normal until the time of her last pregnancy, for which she was again admitted to the hospital in October, 1929, with a history of having been pregnant since the previous May. At this admission a diagnosis of abortion was made, but no operation was performed, and this time she had a macerated fetus. Since then she has menstruated regularly, every four weeks, flowing for three days. No attempt at induction was made in either abortion.

I think a great deal of success in this type of case depends on the technic used. We use two tubes of radium of 50 mg. each, in tandem form, in a brass capsule covered with rubber, so that the entire cavity of the uterus is radiated from the fundus down to the cervix, and we think a very important part of the technic is that the radium when it is placed in the uterus should be anchored there. I am sure

that some of the results which have not been satisfactory are due to the fact that the radium has not been fastened in situ. We anchor it with a silk thread attached to the tube and to a needle, which is passed and held taut by the assistant while the vagina is packed with gauze. It is then sutured to the perineum and tied. When removed, the interne cuts the knot at the vulva and withdraws the gauze and the attached radium.

We have an electroscope in the operating room with which we test the radium, thus proving its presence in the container. We think the packing with gauze is important. The vagina should be distended to the utmost so as to push the bladder and rectum as far away from the radium as possible and thus get the value of distance screening with much less irritation of the bladder and rectum. The use of the self-retaining catheter is most important.

I think the gynecologist should know how to use radium. It is very true that radiologists are necessary for their part of the work, but we certainly feel that it is the clinician's job to know how to use radium, and he should be familiar with its dangers as well as with its advantages.

DR. HOWARD C. TAYLOR.—The limitation placed by Dr. Phaneuf upon the size of fibroids suitable for the use of radium seems to me a very proper one, for tumors larger than the uterus of a three months' pregnancy, as well as pedunculated and submucous tumors are not well controlled by radium.

The use of radium in young girls seems to me a dangerous procedure both from the possible effects on the endometrium as well as from that of a permanent damage to the ovaries themselves. If radium is employed in such patients, it must be only as a last resort and should certainly be administered in the manner outlined by Dr. Ward, in very small doses repeated if necessary.

The dosage for fibroid of the uterus apparently employed by Dr. Phaneuf was in some cases as much as 1800 mg. hours. This is nearly twice the amount I ordinarily use and, I believe, much more than is necessary.

Dr. Phaneuf spoke also of allowing his patients out of bed a day after radium has been used. Those of you who have performed hysterectomy for cervical cancer a few days after the use of preoperative radium will remember the engorged, edematous condition of the peritoneum at that time. There is no doubt that a similar reaction takes place in the peritoneum after the use of radium for fibroids or for menopausal bleeding and for that reason it is better for the patients to remain in bed for several days after the use of radium until the reaction has at least partly subsided.

In particular I wish to emphasize a point brought out by Dr. Ward that it is no longer possible to do proper gynecology without radium at hand. The technic of its use is simple, is rapidly becoming standardized and is easily learned. Large quantities of radium are not necessary for although we possess 140 mg. at the Roosevelt Hospital, we rarely use more than 100 mg. at a time. The initial expense is not great and will prove a good investment to the hospital and a saver of time to physician and patient. The time to decide whether radium is indicated is not in the office but in the operating room after the curettage has shown the condition of the endometrial cavity. For this reason the plan of renting radium in advance for certain cases will not permit flexibility of judgment and will not tend to the best results. For the same reason the sending of cases picked preoperatively as favorable for radium to special radium institutions is not based on practical considerations.

DR. WILLIAM P. HEALY.—It is interesting that Dr. Phaneuf had so few fibromyomas for treatment by radiation therapy and such a large number of benign bleeding cases in middle life. I do not just recall the age limit he set for middle life or whether he mentioned it, but my reaction to the dosage used was similar to that of Dr. Taylor; that is, that it was probably much greater than would really be

found necessary to bring about cessation of bleeding, and in middle life of women, say from thirty-five to forty-five, certainly a large number of those women would be better off if they did not lose their menstrual cycle. I am not at all convinced from personal observation, that an artificial menopause is a happy experience for the average woman. As a matter of fact most of them complain bitterly about it. Therefore, I think we should attempt something better because we can do better with radiation therapy in the absence of tumors. I would like to encourage the use of smaller doses of radium in instances of uterine bleeding of benign origin in women in middle life not associated with tumors. In the presence of fibroid tumors I think you can also obtain good results in uteri in which the tumors are not larger than a three months' gestation. I believe radium should be used in a dose that will not exceed in tandem form 600 or 700 mg. hours with each capsule. I feel it is rather undesirable to use more than 600 or 700 mg. hours with each capsule in benign conditions, because you can very easily obtain ulceration of the uterine wall, and that will produce persistent leucorrhea and pain, cramplike pain that makes the patient quite unhappy.

I also agree entirely with Dr. Ward and Dr. Taylor in regard to the young woman at the time of puberty or up to the age of twenty years. I hesitate a long time before using radiation therapy in those cases. We resort to all possible methods of medical therapy before resorting to radiation therapy because as a matter of fact we seldom find any pathology in these uteri. Curettage does not give us any information that is of special value, and exploratory celiotomy does not reveal any abnormality. We have done exploratory celiotomy in some of these cases with the idea that there might be some pathology in the ovary, that the capsule of the ovary seemed hard and thick. Finally, when we felt it was necessary to use radium we kept the dose down to 300 mg. hours. We have not exceeded that as our primary dose in any of these young women. Of course, if you only use that dosage it will be weeks or several months before you can obtain the histologic change that goes with the use of radium. If the patient has menorrhagia in the first, second or third period after treatment, you must not think you have failed and give immediately another dose of radium because then you are going to get a cumulative effect and instead of getting 300 mg. hours you get 600 mg. hours, or its effect, if you give 300 mg. hours each time. Six hundred milligram hours is altogether too much to use, we believe, in any young woman under eighteen or twenty years of age, at least six months' time should elapse between the first 200 or 300 mg. hours and a repetition of that treatment.

DR. J. A. CORSCADEN.—I suppose it would be a startling statement to assert that this is a much more important subject than cancer of the uterus, but the mortality statistics in the registration area show that nearly two to three times as many women die from benign tumor as from carcinoma because of the frequency of the disease. From the standpoint of sickness we find that the large employer of women in clerical jobs takes cognizance of menstrual disorders, and it is the common practice to give women one day a month off from work without reference to sick leave or vacation, which means about a 5 per cent loss which is, nowadays at any rate, quite a lot of interest. So I think the details of this treatment, this question of dosage, which has received so much discussion, is of great importance. I would agree with Dr. Phaneuf on the dosage. We have an interesting series of follow-up results. In the women who received 1200 hours the bleeding was controlled in 85 per cent of the cases, whereas in the cases where 1800 mg. were given it was controlled in 97 per cent of the cases. That is to say of the 1200 mg. cases 1 in 7 or 8 required subsequent treatment of some kind or other for the bleeding itself.

In regard to menopause symptoms: in our cancer clinic we have made an observation which is at present only an impression which I hope to be able to record more

accurately later on, that women who receive 6000 to 8000 mg. hours of radium have less menopausal symptoms than those who get only 1500 or 1600.

In some women around 40 years of age at present we are not only giving 1800 but 2400 to 3000 mg. hours filtered with a millimeter of platinum. We feel justified in that by our observations on our cancer cases, whether they are true or false.

In regard to the use of radium in older women: we have been very apprehensive about applying radium to older women, because we have been impressed with the association (it may be remote) between the hyperplasia coming on after the menopause and carcinoma. In women in perfect health sixty years old who are bleeding, even without a definite diagnosis of adenocarcinoma, we would be inclined to do a hysterectomy rather than apply radium.

I have two very interesting benign cases. One of them had a bilateral salpingo-oophorectomy at forty-seven. At the age of seventy-three she suffered from periodic hemorrhages every two or three months. An attempt had been made to remove the uterus because of a suspected carcinoma. She was referred to us for palliative treatment, dilatation and curettage revealed a luxuriant hyperplasia. We put in 1800 mg. hours of radium with no effect on the bleeding whatsoever. She is now eighty-four years old. She goes on bleeding every two or three months and is in perfect health as far as her pelvic organs are concerned. I simply cite that as one of the odd cases of uterine hemorrhage which may have a local cause. At any rate, we think that the use of radium therapy for hemorrhages following the menopause is likely to be followed years later by trouble.

DR. WALTER T. DANNREUTHER.—I cannot agree that it is necessary to use radium at all for menorrhagias of adolescence. I was surprised that Dr. Phaneuf did not mention the associated endocrine and constitutional disturbances, which are so important in these cases. I have had a number of young patients with profuse bleeding and have been impressed by the manifestations of thyroid dysfunction in a large proportion of them. As a general rule, it is one of the first things noted, and is more often a hypo- rather than a hyperthyroidism. Knowing the reciprocal co-operation and influence of the pituitary, thyroid and ovary in the promotion and control of menstruation, I do not think it strange that endocrine imbalance is often found to be a causative factor. Sometime ago I developed a routine of treatment which has served me in such good stead that in no single instance have I failed to arrest the abnormal bleeding. Usually by the time the patient comes under observation she is somewhat exsanguinated, and has a secondary anemia, a hemoglobin of 25 to 50 per cent, a low red cell count, persistent bleeding, and a distracted family. It is desirable to have a basal metabolism test done, as this, together with a survey of the patient's physical characteristics and history, enable one to form a definite idea of her endocrine status. She is then given a transfusion of 300 c.c. of blood. Calcium is administered by mouth and sometimes intravenously. Soon thereafter the patient is referred for x-ray of the spleen, never the plevis. At the Post-Graduate Hospital we give approximately one-quarter of a skin erythema dose, repeated at three or four week intervals. Hypodermic injections of iron arsenite and strychnine and a high caloric diet, with appropriate organotherapy are valuable adjuncts. Two or three transfusions, two or three or four applications of x-ray to the spleen, and general constitutional measures, plus organotherapy, have eventuated in a satisfactory result without exception. Such a case was a girl of fourteen with persistent bleeding for six weeks before admission and hemoglobin of 25 per cent. She was treated in accordance with the suggestions outlined and her bleeding was entirely controlled in about three weeks. A diagnosis of hypothyroidism could almost be made by placing the hand on the patient's abdomen, as the skin was like parchment. Once such a clue presents itself, one has only to look for additional evidence. In such a case, if the patient has falling hair, a slow pulse, is mentally sluggish, is sleepy dur-

ing the day, and has other symptoms pointing to hypothyroidism, the diagnosis is established.

It is well to emphasize the desirability of being patient in evaluating the end-results after radium therapy in benign cases, in both the younger and older women. It is advisable to caution the patient in advance, that the permanent effects of the radiation may not be established for three to six months, and that a transitory leucorrhea often follows the irradiation. This is sometimes quite irritating, unless an alkaline douche is taken daily.

DR. IRA I. KAPLAN.—In a free hospital such as Bellevue irradiation therapy is mostly used for malignancy. Occasionally benign conditions are referred for treatment but most of these have been treated unsuccessfully elsewhere and are then sent to the gynecologic service at Bellevue for whatever saving methods we may be able to apply. Most of these cases have been curetted a great many times and for that reason irradiation with radium acts so well in small doses and, in as much as a great deal of the endometrium has already been destroyed, there is very little left to take care of with the radium because most of the capillary tissue is gone.

If radium is used it is important to place it in the whole uterine cavity. In our experience with radiation therapy, we have found that the treatment of uterine bleeding can be well carried on without packing radium into the uterus, and in the case of young women, why should we destroy an active uterine endometrium? If we believe that uterine bleeding is in most part an ovarian function and in part and endocrine function, why not control this bleeding in some manner without destroying the endometrium of the uterus which, especially in the case of young people may be required later on. In the exceptional case pregnancy may occur after radium; the usual case with a destroyed endometrium seldom becomes pregnant.

I agree with Healy, that early menopause is not a pleasant thing for women. You can avoid that. In our cases, of which we have had several hundred, we have found that the women under fifty cannot always be castrated with the x-ray and women under twenty castrating is never permanent, and occasionally definite in women between thirty and fifty. In cases over fifty, x-ray castration always occurs. In girls of thirteen we would not think of using radium. In such cases we feel that there is a functional disturbance which may be corrected by treatment over the spleen. We always try the spleen first, and then the pituitary.

I am quite in accord with Dr. Phaneuf on the amount of dosage that he uses, especially in the older patients. Not every pathologic specimen is going to show you the true history of the case. Time and again even though the biopsy was reported as nonmalignant, the clinical course of the case proved the lesion was malignant. One of the most peculiar conditions is as Dr. Corseaden has remarked, that in older patients malignancy will hide itself under the old sclerotic covering of an ancient endometritis. Therefore I think we are much safer in using a large dose of radium as Phaneuf does and for a time inhibit the extension of a probable malignancy even if it does not cure it entirely.

DR. HARVEY B. MATTHEWS.—Accurate diagnosis is one of the first and most important steps in the use of radium. We have seen a few cases in which radium was used where it was contraindicated; as for example in the presence of chronic inflammation with small adnexal masses or slight parametrial induration. These latter lesions may be overlooked when one is in a hurry due to stress of work or is careless in making pelvic examinations. There is no question but that radium does excite activity in these chronic pelvic inflammations.

Smaller doses given over a period of six months' time will give better results than one large dose such as Phaneuf has recommended. For the middle-aged or older lady 1200 to 1500 mg. hours is usually what we give, sometimes when pregnancy is to be considered 600 to 800 mg. hours, and repeated if and when necessary.

In regard to the dosage in young women: we start with 200, 300, or 400 mg. hours, and in the young woman under twenty years we prefer to use one, two, or even three small doses.

From our laboratory experiments in rabbits, where we radiated the ovary up to 800 mg. hours in one dose; or 800 mg. hours in two doses over a period of four months, we are convinced that such dosage is perfectly safe as far as pregnancy is concerned.

DR. WILLIAM S. SMITH.—I am very much interested in the group of cases that the doctor reports, because we have a similar group of cases in our series at the Brooklyn Hospital. We have 111 metritis cases, all of which were over forty years of age. We have 34 cases of fibroids. In the beginning our dosage was 1200 mg. hours, but as there were five women who began to flow again, we gradually increased the dosage to 1800 mg. hours, and now the majority of metritis patients are given 2400 mg. hours. We screen our radium with one full millimeter of platinum. With heavy screening and large doses we have had little or no trouble from leucorrhœa. We have had no trouble whatsoever in these 111 cases of chronic metritis from irritation of the bladder or rectum.

We do not use a self-retaining catheter, and have never had any difficulty from a distended bladder. If the patient cannot void she is catheterized, and with the radium heavily screened we do not fear irritation of the bladder. We use the radium in two capsules, each of which contains 50 mg. We fasten the capsules in tandem within a rubber tube and place it high up in the uterine cavity. We pack the cervix with a narrow strip of plain gauze, in addition to firmly packing the vagina.

We have had 15 cases in this series of 111, in which there have been various surgical operations, such as amputation of the cervix, trachelorrhaphy, anterior colporrhaphy, and perineorrhaphy. In these cases we do not pack the cervix or the vagina, but suture the rubber tube into one lip of the cervix with a long piece of catgut. The suture is tied in a single bow knot, and the long end is left outside the vagina. In this way we are sure that the radium remains where it is placed, and in addition, it is very easy to remove the suture and the radium. Our surgical results in this group of cases have been uniformly good.

DR. T. C. PEIGHTAL.—At the Roosevelt Hospital we have had approximately 600 cases where we used radiation for benign fibroids and idiopathic bleeding. In our series there were about 55 per cent of fibroids and 45 per cent of idiopathic bleeding.

For fibroids in general we have found that roughly only about 10 per cent of them were suitable for radiation. Of the other 90 per cent approximately 65 per cent had some type of hysterectomy; while in the other 35 per cent menstrual function could be maintained by myomectomy or partial hysterectomy. For cases of idiopathic bleeding in general we found that 65 per cent needed only curettage; and about 35 per cent of this group were radiated.

In regard to the technic of radiation we use either 50 mg. in one capsule or two 25 mg. doses in tandem, or if the cavity is long enough one can even use 50 and two 25. In other words, we vary the capsules of radium according to the size of the uterine cavity. I think that is an important point to bring out. The radium is placed in special rubber tubing free from metallic content and this tubing is held in place by a suture through the lips of the cervix. As all the radium is well up in the fundus, we do not pack the vagina and, therefore, practically all of these patients void, and the very few who do not are catheterized. I know of no cases of bladder or rectal complications from this procedure.

We started in 1917 with a dosage of 500 mg. hours, even in fibroids. This was gradually worked up to about 1500, and now it has gone down the scale again, until today, in fibroids that are suitable for radiation about 700 to 900 mg. hours is all



that is used. In other words, after experience with higher dosages we believe just as efficient results can be obtained with the lower ones.

DR. LOUIS E. PHANEUF.—Dr. Ward's greater experience than mine, 309 cases, bears out a number of points which I have mentioned. He uses smaller dosage than I have employed in the very young woman, I will be guided by this in the future. If, however, the hormones of the anterior pituitary body and of the ovary come up to our expectations we may find a new solution to these cases which will make radiation unnecessary. Ward advocates the use of the self-retaining catheter as I do, and feels that it is safer to keep the bladder flat and absolutely empty. Distention of the vagina, with gauze, I have practiced in this series of cases as he has described.

Dr. Healy claimed that I had used doses larger than might be necessary. I have felt my way with these cases, and, like Drs. Corseaden and Smith, have found that after a 1200 mg. hour dose occasionally I met repeated bleeding which was very distressing to the patient. I have crept up to 1800 mg. hours, but, like Peightal, I am getting back to a smaller dose as time goes on.

In answer to Dr. Corseaden I would say that 11 different types of operations were performed on 44 women in conjunction with the insertion of radium, curettage, amputation of the cervix, perineorrhaphy, etc. These operations have given me satisfactory results in all cases. I have not found any difficulties following them nor have I found any secondary hemorrhages. Therefore, I would not hesitate to amputate the cervix when necessary.

I agree with what Dr. Corseaden said in regard to older women; hysterectomy is preferable to radium. I usually do a vaginal hysterectomy in these older women to get rid of the bleeding uterus. In some of the cases I had, there were constitutional contraindications to hysterectomy. I felt that radium was safer than vaginal hysterectomy even though that procedure is attended by very little shock.

Dr. Taylor has emphasized the danger of using radium in young girls and also the smaller dosage, which is in keeping with the general trend of the discussion. Like Dr. Ward he advises 300 or 250 mg. hours. My impression was from Dr. Matthew's first article he had published on the subject that he had found a dose up to 800 mg. hours to be within safe limits. The tendency today is to give smaller doses.

Like Dr. Dannreuther I feel that young women with irregularities of menstruation should be studied medically and endocrinologically. We have, in our hospital, a man who is especially interested in endocrinology who studies these cases as completely as possible. In those which I have reported all the tests mentioned including basal metabolism had been carried out. Treatment along these lines had been administered without success and when the bleeding became alarming radiation was resorted to.

I have had but one experience with x-ray application over the spleen. I was not able to follow the results as this patient had a hysterectomy done by another surgeon.

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## OBSTETRICAL SOCIETY OF PHILADELPHIA

MEETING OF DECEMBER 3, 1931

DR. JAMES P. LEWIS reported a case of **Cornual Pregnancy**.

The classification of the type of extrauterine gestation found at operation or autopsy is not always a simple procedure. This case clinically shows many features of a cornual type, but the autopsy findings rather suggest a well advanced tubal pregnancy.

The patient I. A., para ii, aged twenty-one, colored, was admitted to the service of Dr. Philip Williams at the Philadelphia General Hospital, July 8, 1931. Her chief complaint was pain in the lower abdomen. Her last menstrual period was on March 16, 1931. Ever since she had stopped menstruating she had continuous pain in her lower abdomen, not severe enough to put her to bed. On July 5 patient had a sharp lancinating pain in the left lower quadrant of the abdomen so severe as to make her feel weak and cause her to go to bed for that day. On July 8 she had a similar attack of very severe pain, and she was sent to the hospital.

On admission to the hospital the patient was *in extremis*. Temperature 97°, pulse 140, respirations 40. She was markedly anemic and in shock. Pelvic examination revealed a multiparous outlet but with good support. There was no vaginal bleeding. The cervix was slightly softened. The uterus seemed uniformly enlarged to the size of a four months' pregnancy. The body of the uterus could be felt 2 fingers-breadth below the umbilicus. There was tenderness over the body of the uterus and some tenderness on motion of the cervix. There was no tenderness in the adnexal regions nor were any lateral masses palpable.

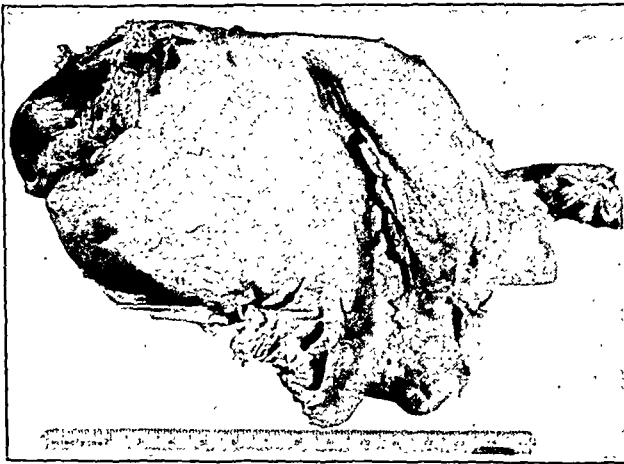


Fig. 1

Inasmuch as the size of the uterus corresponded to the period of amenorrhea and there were no masses in the adnexal region, rupture of an ordinary tubal pregnancy seemed unlikely, and a tentative diagnosis of ruptured uterus and probable cornual pregnancy was made. The patient's condition made hysterectomy impossible. Notwithstanding active and vigorous treatment she died within two hours after admission.

Autopsy revealed the peritoneal cavity markedly distended by free and clotted blood which displaced the diaphragm upwards. The cervix uteri was enlarged and soft. The uterine cavity itself was but little enlarged. At the extreme upper and outer left corner of the uterus was a large sac whose covering was continuous with that of the uterus. It contained a fetus of about three months' development. The amnion was intact, holding the amniotic fluid. The surrounding membranes were ruptured leaving a markedly bloody surface. The ovary of the left side was not found. The right tube was of small caliber and would not allow a probe to pass through its lumen. The right ovary was normal.

Fig. 1 illustrates the findings much better than the pathologist's description. Grossly and clinically this appears to be a case of cornual pregnancy, but it lacks

certain criteria. The left tube was not identified outside the gestation sac. Whether the sac which is continuous with the uterus is an enormously enlarged tube which ruptured at the fimbriated extremity must still be decided.

DR. W. B. HARER presented a paper entitled **A Study of Fetal Mortality**. (For original article see page 254.)

#### DISCUSSION

DR. E. B. PIPER.—The high mortality shown on some of these charts was sometimes largely a question of knowing the child was lost on admission, and too late for a cesarean section safely. Therefore they were treated as seemed best in the eyes of the individual doctor. We do not believe there is any routine way.

As for the statements made about out-door obstetric services, I desire to state that the fourth-year medical student of today is a great deal better prepared to take care of obstetric cases in private homes than were many of the older men when they received their degree in medicine. The fourth-year medical student is trained to be able to diagnose and send in bad cases. In a series of four thousand and some hundred cases in the Southeastern Dispensary of Philadelphia, the mortality of the cases handled by students was 2.2 per cent.

DR. WILLIAM R. NICHOLSON.—I am thoroughly in favor of the statement made regarding the use of forceps in the after-coming head cases. I think there is no doubt that infant death rate is very much reduced by forceps delivery.

DR. JOHN A. McGLINN read a paper entitled **Reconstruction of the Urethra**. (For original article see page 262.)

#### DISCUSSION

DR. EDWARD A. SCHUMANN.—Cases of reconstruction of the urethra may be divided into two groups. One group includes the fundamental cases, the other those of traumatic origin.

The first group, of hypospadias cases, are always connected with an insufficient blood supply, and in them reconstruction is much more difficult because of the danger of anemic tissues breaking down.

The second group offer an almost equally strong objection to closure, in that most of them have suffered so many attempts at repair, and the vagina has been reduced to a mass of fibrous tissue.

In one case in which I attempted the Ward technic with a reasonable degree of success, the bladder fistula was so large that I felt I could not get a wide enough flap of tissue to close it. I therefore made a successful attempt to reduce the size of the bladder tissue, and this method has now become habitual with me.

DR. F. H. MAIER.—It has been our practice to correct through the suprapubic Pfannenstiel incision urinary fistulae which were difficult of correction through the vagina and which had been unsuccessfully operated upon before.

DR. J. H. GIRVIN.—I have recently had two reconstructions of the urethra and had rather unfortunate results in both cases. The first I have operated upon at least fifteen or sixteen times. We gradually closed the opening of the bladder, and then reconstructed the urethra, but of course with no muscular control. This looked so favorable that I determined I would bury some muscle fiber around the urethra. I used fibers of the levator ani muscle, and got a very successful result; but she left the hospital with a rectovaginal fistula which I have not yet been able to close.

The other case was a comparatively large vesicovaginal fistula, in which I had a very successful result with the first operation. She came back with a very small opening not much larger than the point of a pencil. Following the attempt to close that, the whole of the lower half of her urethra sloughed away, and I have done at least eighteen other operations in the attempt to correct this condition.

I think one important factor is not to use absorbable sutures. I got much better results from using a very thin silkworm gut.

DR. LEONARD AVERETT.—I was called in consultation to a patient who had been in labor for forty-eight hours with a contracted pelvis making vaginal delivery impossible. I performed a cesarean section and five days later patient began to dribble urine from the vagina. Upon examination, I found the anterior portion of the cervix sloughed away and a hole in the posterior wall of the bladder just above the trigone. This was due to a pressure necrosis as result of the prolonged labor.

The patient made an uneventful recovery and returned seven months later for repair of the vesicovaginal fistula. After repair of the bladder, a self-retaining catheter was inserted for continuous bladder drainage. A week later the incision broke down and she again began to dribble urine from the vagina. When she was discharged from the hospital she was advised to return in four months for another operation. A month later she presented herself at my office for examination and I found the fistula entirely healed.

DR. F. H. MAIER AND DR. W. J. THUDIUM presented a paper entitled  
**The Fothergill Operation.** (For original article see page 248.)

#### DISCUSSION

DR. JOHN M. FISHER.—It appears to me that the Fothergill operation is founded upon correct anatomic and physiologic principles. As I have seen it done by Dr. Maier it apparently meets the indications referred to in a very large proportion of cases. Nevertheless, in the absence of more enlightenment on the subject I should hesitate to accept it as a standardized procedure for all cases of uterine prolapse.

Dr. Maier claims that the more pronounced the prolapse the greater the adaptability of the operation to the condition. I should like to see him operate on a case of procidentia with a complete inversion of the vagina and note the result six months later.

DR. GEORGE OUTERBRIDGE.—I should like to ask Dr. Maier just what the result after this operation is with regard to the cystocele that usually accompanies prolapse? I could not see from his description that anything was done to correct it, and my feeling was that, just as has been stated by Dr. Hirst, it would be apt to give trouble.

DR. GEORGE LAWS.—In England the conception of the mechanism of genital support is different in that it is believed to depend almost wholly upon the connective tissue sheaths of the blood vessels.

I have done two or three of these operations with success, but felt that it was contrary to the best teaching, though the simplicity of the procedure commends it.

DR. JOHN A. McGLINN.—I am in thorough accord with everything that Doctor Maier has said, except to speak of the Fothergill operation as a standardized operation for prolapse of the uterus. I do not believe you can have such a thing as a standardized operation. The surgeon must be prepared to meet the various conditions and complications that are present in prolapse of the uterus. There is no

doubt that this operation does cure prolapse. It is easy of execution and I have done it successfully under local anesthesia.

There are cases of prolapse, however, in which it would be a serious error to leave the uterus behind. A uterus that is in any way suspicious, particularly after the menopause, should be removed.

DR. LEONARD AVERETT.—I have performed the Fothergill operation twice. The results were very good in both cases and I am very much impressed with this operation. In both cases, I had a large cystocele to deal with and after dissecting the bladder from the cervix, I anchored it higher up, which I believe differs from the original technic.

DR. MAIER (Closing).—Any one familiar with the technic and the results of the Fothergill operation cannot help but be impressed with its superiority over all other methods for the cure of uterine prolapse.

It eliminates the opening of the abdominal cavity with its attendant percentage of mortality and morbidity and prolonged convalescence. Unlike the interposition operation it is applicable to women of all ages, as the retention of a three-inch uterus permits childbirth.

Diagnostic curettage is performed routinely. We believe that correction of the cystocele can always be accomplished by removing a sufficiently large triangle or quadrangle of vaginal wall. In some cases of elongated cervices in women beyond the menopause we push the bladder well up off of the cervix and amputate as high up as possible.

In answer to the question of how deep we introduce our needle into the paracolpo-metrial tissue: we go through the vaginal walls only. The closure of the wound brings and holds the tissues in front of the cervix. The cervix is thereby pushed upward and backward into the hollow of the sacrum, leaving the uterus in the much desired position of anteversion.

DR. JOHN C. HIRST reported a case of **Microcephaly**.

This example of a microcephalic newborn infant is presented because unusual familial circumstances offer favorable opportunity for discussion as to the causative factors and mode of development involved.

This abnormal infant was born to Mrs. E. A. in the obstetric service of the Burlington County Hospital, Mount Holly, N. J., July 3, 1931. Patient was white, aged twenty-six, one of twenty brothers and sisters, twelve of whom are living, but all feeble-minded. The father, one of seven children, only two surviving, orphaned at two years of age, was "raised" by an aunt who later became insane. Living a primitive life in the New Jersey wilds, the parents, working only when forced, typify certain of the "Pinneys," namely, those astounding half-wild illiterates to be found near by in the bogs and pines of New Jersey, who if, as many believe, originated as refugees from stringent religious law of fine Quaker stock, certainly show no present resemblance to their forebears. The father particularly suggests the degenerate, whose main emotion being one of sex, becomes aroused even by lower animals.

Mrs. E. A.'s history is featured by very short, scant, but regular and painless menses, no miscarriages, six prior births, the last three with transverse presentation and prolapsed arm, only one surviving.

Physical examination revealed nothing unusual as of time of this birth for which the patient was admitted in labor, membranes intact, rectocele and cystocele, no obstruction yet floating head in the iliac fossa, for which version and extraction were performed without complication.



Fig. 1



Fig. 2

The female infant, length 46 cm., well developed mature body, weight  $6\frac{1}{2}$  pounds presented an obviously small cranium, small fontanelles, cranial bones firmly united at prominent sutures and a startling appearance mainly due to mature facial expression with prominent active eyes and lids resembling somewhat the frog facies of anencephalus.

## HEAD MEASUREMENTS

		WHITES-NORMAL
Occipitofrontal	9 cm.	(11.75)
Biparietal	7 cm.	(9.25)
Bitemporal	5 cm.	(8.0)
Occipitomenal	$10\frac{1}{2}$ cm.	(13.33)
Suboccipitobregmatic	$7\frac{1}{2}$ cm.	(9.7)
Circumference	22 cm.	(34.50)
(Chest Circumference)	27.9 cm.	(33.25)

X-ray examination revealed no skeletal abnormality, but a brachycephalic type of moderate microcephalus with very poor development in the region of the occiput and foramen magnum.

A negative Wassermann was found in child and mother. Decidedly peculiar actions and increasingly unusual appearance strongly suggested idiocy; poor nursing; weaning and unsatisfactory weight. At the age of five weeks, following discharge from the Maternity, the infant was readmitted to the pediatric service for vomiting and extreme emaciation, when the disproportionally small cranium was again more striking than the diameters indicated, and probably the underlying cause of death on August 31, 1931. No postmortem examination.

My review of more than twenty thousand consecutive birth records from the Southeastern Dispensary Out Service of the University of Pennsylvania Department of Obstetrics, shows that hydrocephalus unlike hemicephalus, affected the colored infants more often than white, distributed equally between male and female newborn, so that it is more than likely that relative hydrocephalus has nothing to do with microcephaly and even hemicrania, especially since in the above series only white infants (mostly female) showed the latter anomaly.

The only treatment of microcephaly available is based on a theory of unyielding sutures and poorly developing skull bones, namely excision of cranial bony strips, which as far as known (Birnbaum) has been ineffectual.

# Department of Reviews and Abstracts

CONDUCTED BY HUGO EHRENFEST, M.D., ASSOCIATE EDITOR

## Collective Review

### A Critical Review of the Gynecologic Literature of 1931

JULIUS E. LACKNER, M.D., AND SYDNEY S. SCHOCHET, M.D., CHICAGO

#### INTRODUCTION

THERE is a general law that progress in any direction is characterized by specialization. This is brilliantly exemplified in the specialty of gynecology. During its early history we note the remarkable development of operative procedures which general surgery perhaps never would have accomplished. Following this period there came a narrow and ineffective study of gynecologic diseases based on the morphologic pathology of the pelvic structures with its attendant classification of endometrial lesions as hyperplastic and hypoplastic endometritis et cetera. Finally it became apparent that the correct interpretation of the many gynecic problems must be based on physiologic processes and their interrelationship with other organs and the ductless glands rather than on histologic changes in the reproductive system. Physiologic studies and this most recent attitude toward gynecology are the outstanding topics of the gynecologic literature of 1931.

#### GENERAL PROBLEMS

Gynecology is becoming less and less a purely surgical specialty. Emil Novak<sup>1</sup> reviews the development of gynecology and rightly emphasizes the necessity of a thorough knowledge of the physiology and pathology of the reproductive apparatus in clinical studies. In an analysis of the biologic significance of the female reproductive cycle he emphasizes the phenomena of periodicity as exhibited in the functions of the female reproductive organs. Periodicity may be said to be a rule of the universe. Graves<sup>2</sup> maintains that the ultimate goal of pure science is the complete unification of all the laws of nature into a single principle which shall explain the phenomena both of living and nonliving matter. The goal of applied science is to utilize the knowledge thus gained in ways that may benefit the human race.

Every gynecologist should be trained in pathology or at least have a comprehensive knowledge of gross pathology. In all but the most exceptional hospitals the surgeon must depend upon the pathologist and accept his decision for the course of operative procedure. This interdependence of the pathologist and surgeon is presented in a most forceful editorial by Maes.<sup>3</sup> (In our experience we have not always found the general pathologist sufficiently trained and versed in gynecic pathology.)

Not infrequently patients with faulty calcium metabolism and abdominal spasmophilia are subjected to abdominal operations though they only needed an increase of the blood calcium.<sup>4</sup>

A most instructive and valuable contribution on the effect of intravenous glucose on cardio-vascular apparatus and cellular contents of the blood is presented by the late John O. Polak.<sup>5,6</sup> Nafe<sup>7</sup> outlines the more common causes of postoperative complications of abdominal operations and the methods of treatment.

Since Cullen's first report of postoperative gangrenous ulcer of the abdominal wall fifteen others have been recorded in the literature. Lynn<sup>8</sup> is of the opinion that this pathologic process occurs even more frequently than would appear from the literature. The gangrenous process usually begins a week or two after the operation; the specific etiologic factor has not been isolated; and the ordinary germicides and antiseptics are not effective in checking this condition. The use of the cautery gives the most prompt and encouraging results. Hypertonic solutions of sodium chloride appear to be effective.



Schmidt<sup>9</sup> reports that in the women's clinic of the University of Breslau out of a total of 6,114 gynecologic operations, 134 (2.19 per cent) developed thrombosis, and 26 (0.42 per cent) died of pulmonary embolism. Chaliér<sup>10</sup> believes that phlebitis after gynecologic operations is usually aseptic, and that the suppurative lesions such as pyosalpinx give the veins an immunity through autovaccination. (This view is borne out by clinical evidence.)

Masson<sup>11</sup> reports on 313 operations for low median incisional hernias at the Mayo Clinic. The predisposing cause of hernia in many cases is a previously infected wound, but hernia may develop also without preceding infection. (In our service we prefer the routine Pfannenstiel incision which is the ideal prophylactic measure.)

The subject of anesthesia is discussed in more detail in another section of this review. Roeder<sup>12</sup> states that spinal anesthesia produces respiratory failure in two ways: a paralysis of the motor nerves of respiration and a paralysis of the vaso-motor nerves of the splanchnic area, which cause a fall of bloodpressure followed by myocardial and medullary ischemia. A five or ten per cent by volume of carbon dioxide in pure oxygen is suggested as an adjunct when the motor nerves or the muscles of respiration are not paralyzed. (Our conception of anesthesia is that synthetic procain groups unite directly with the protoplasm of the cells and therefore are protoplasmic poisons.) In a discussion of narcotics in obstetrics and gynecology, De Lee<sup>13</sup> presents a very exact and detailed outline for the use of such drugs in postoperative conditions.

Deneks<sup>14</sup> suggests that the appendix be removed in all gynecologic operations, as it is often found to be the causative factor of dysmenorrhea. According to Howard Kelly<sup>15</sup> electro-surgery in gynecology has not received the attention this method deserves.

In a study of the positive Wassermann reaction in gynecologic surgery, Scheffey<sup>16</sup> finds that the incidence of syphilis in the operative cases as indicated by a positive test was 8.6 per cent.

In the entire range of subjective gynopathic manifestations, backache is one of the most familiar and least understood as to its nature, its direct cause, and the mechanism of its production. Sturmdorf<sup>17</sup> believes that gynopathic backache is a spastic backache, the gynopathic factor being one among many causes of myospastic pain in the lumbosacral area, and that this myospasm is a protective phenomenon. Like most other authors Young<sup>18</sup> attributes the low back pain to lumbosacral or sacroiliac strain. (We are of the opinion that many of these cases are due to pelvic congestion or pressure on the lumbosacral nerves with the resultant myospasm. Nevertheless we are not blind to the fact that a certain percentage of the cases must be attributed to the lumbosacral or sacroiliac joints.)

Templeton, Stein and Schochet have found that there are rhythmic contractions of the vagina and that an alteration in this physiologic function may be the cause of frigidity or dyspareunia. Leigner<sup>19</sup> believes that primary dyspareunia is due to a defect present in the genitals. (Physiologic studies do not confirm these views.)

It still is a moot question whether sex instructions should be imparted to children with the present overemphasis as advocated by many writers on this subject.<sup>20, 21</sup> Dickinson<sup>22</sup> is of the opinion that there should be schedules for sex education, for premarital medical instruction and texts on conjugal hygiene—as a program for preventative gynecology and protective medicine. (This contribution deserves careful study by gynecologists.)

In a somewhat revolutionary reclassification of pelvic lesions, Kisel<sup>23</sup> advocates a grouping based on "an absolute symptom complex" and claims that the laboratory is in a position to differentiate all diseases by this method. (We purposely mention this paper to show that there appears to exist a trend in medical thought and education of Russians which harmonizes with their social experiments.)

In a study of 1516 postnatal patients, Lash<sup>24</sup> finds that the symptoms of headaches, dizziness, and backache were the most common, and that these symptoms were often associated with retroversion. The author advocates the correction of the retroversion, and when this is associated with a relaxed perineum, he suggests a series of exercises, and massage for increasing the tone of the levator muscles.

Under proper conditions psychotherapy plays an important rôle in gynecology.<sup>25, 26</sup> Mayer<sup>27</sup> in a study of a series of cases from the gynecologic service of Mount Sinai Hospital presents conclusive evidence that such psychic investigations often clarified operative indications and eliminated almost entirely certain types of operation.

Each year many new laboratory tests are suggested to the gynecologist as aids to diagnosis and treatment. Molfatti<sup>28</sup> emphasizes the significance of calcium in the organism; Volter and Sharovskaya<sup>29</sup> discuss the important relations of lipase of the blood to infections; Hueper<sup>30</sup> et al. stress the value of the malignancy indices,

and the blood  $P_H$  values, and De Gaetani<sup>31</sup> writes of a method of inducing resistance against malignant tumors. All these suggestions may have real significance but in our present state of knowledge it is difficult to make a proper evaluation of these claims. Gay<sup>32</sup> presents a very interesting discussion on the subject of tissue resistance and immunity and attempts to correlate changed functional activity with structural alteration. Mullin and Large<sup>33</sup> see much value in studying the filament and nonfilament white cell count—a modification of Arneith's classification of polymorphonuclear blood cells. Mathieu<sup>34</sup> and Osgood<sup>35</sup> et al. have modified and improved the technic of the sedimentation test. (It is of special significance to one of us that *trichomonas vaginalis vaginitis* a type of specific infection does not alter the sedimentation time.)

#### ANESTHESIA

In most instances the anesthetic is as important as the operative procedure. Leaders in medicine and surgery rely upon the anesthetist to choose the method best suited to the individual case, to prevent accidents, and to insure the patient's recovery.<sup>36</sup>

Ether anesthesia is associated with hyperglycemia due to mobilization of the hepatic glycogen. According to Mekie<sup>37</sup> the action of ether is probably direct upon the liver cells. Pernocton injected intravenously may be used as the sole anesthetic or to reduce the amount of inhalation anesthesia. According to Brown, Moloy and Laird,<sup>38</sup> it does not cause excitation and post operative nausea is rare. Stander<sup>39</sup> favors avertin anesthesia in those cases in which general inhalation anesthesia is contraindicated and in which there is no evidence of disturbed hepatic or renal function. Avertin should not be given in amounts exceeding 100 mg. per kilogram of body weight. (From reported pharmacologic studies this compound of barbital should be employed with extreme caution.)

According to Falk<sup>40</sup> spinal anesthesia should not be used as a routine in all cases. It should be administered only by a trained anesthetist. Adams<sup>41</sup> found it a safe anesthetic in 88 to 98 per cent of his surgical cases. McKittrick, McClure and Sweet<sup>42</sup> from extensive observations at the Massachusetts General Hospital conclude that spinal anesthesia does not fulfill all the requirements essential to an ideal anesthetic for abdominal surgery, but that it has an important place in surgical work below the diaphragm. There was apparently an increase in the number of postoperative complications with spinal anesthesia. In elderly and debilitated cases this may be due to an increase in the incidence of atelectasis.

Stahnke<sup>43</sup> reports postoperative pulmonary complications in 14.2 per cent of gynecologic laparotomies under ether, and in 17.7 per cent under spinal anesthesia. Anderson<sup>44</sup> urges the necessity of better knowledge of how to combat the persistent headache and the fall in blood pressure subsequent to spinal anesthesia.

Burch and Harrison<sup>45</sup> have shown that the administration of ephedrin to dogs under spinal anesthesia decreased the susceptibility of such animals to hemorrhage, and caused a rise in the systolic pressure. The drop in blood pressure may be avoided by giving salt solution previous to the induction of the spinal anesthesia. Keyes and McLellan<sup>46</sup> claim that the advantages of nupercaine over procaine are greater than the disadvantages. Winograd and Rosenbloom<sup>47</sup> in a review of the literature on spinal anesthesia suggest the possibility of pathologic changes in the spinal cord caused by the anesthetic. Davis et al.<sup>48</sup> have found the following changes in the spinal cord of dogs after spinal anesthesia: (1) a varying degree of inflammatory reaction in the leptomeninges; (2) passive changes in the ganglion cells of the gray matter of the cord; (3) swelling and fragmentation of the axis cylinder; and (4) degenerative changes in the fiber tracts of the cord. The last three changes were not pronounced after ninety days. (This careful study should leave an indelible imprint on the mind of the student of spinal anesthesia.)

Bevan<sup>49</sup> can see no reason for the use of spinal anesthesia. He believes that it is more dangerous than chloroform, not always efficient, is not a comfortable method, does not eliminate psychic trauma, and causes aseptic meningitis. (We appreciate the limitations of spinal anesthesia, but do not concur in these sweeping statements. From our observations at the Michael Reese Hospital, we believe it to be the ideal anesthetic when used in properly selected cases and with proper technic.)

Deaths due to explosion of anesthetic mixtures have been given wide publicity in the lay press.<sup>50</sup> However, statistics show that it is the least of the hazards of anesthesia.

#### BREASTS

As in previous reviews we include a short résumé of lesions of the mammary glands as accessory glands to the organs of reproduction. Schochet, Lackner and Gustavson have shown that the female sex hormone is present in the blood of the newborn, and is the causative factor of mammary activity at birth through the blood stream.

Cutler<sup>61</sup> believes that painful breasts or mastopathy is due to a certain type of desquamation of epithelial cells in the ducts and acini which is accompanied by hyperplasia of pericanalicular and periacinous connective tissue. Cutler is of the opinion that the syndrome of painful breasts is due to an overstimulation of the breast epithelium and connective tissue by the corpus luteum hormone, and that this condition is relieved by oral administration of dried ovarian residue from which the corpus luteum was removed. (In our experimental studies we have failed to observe physiologic results from the female sex hormone by oral administration.)

Seabold<sup>62</sup> concludes that the roentgenogram is a valuable adjunct in the diagnosis of lesions of the mammary gland.

Tuberculosis of the breast is a relatively rare condition when compared with the frequency of tuberculous infection in other organs of the human body. Morgen<sup>63</sup> reports that tuberculosis of the breast occurred in 0.51 per cent of all mammary conditions that were admitted to the hospital at the Mayo Clinic.

In a study of 1347 cases of malignant tumors of the breast, Crile<sup>64</sup> states that the average natural duration of life for a patient with carcinoma of the breast is three years; with radical operation about 38 per cent of the cases will be free from the disease for the natural duration of life, and that the average survival for five years will amount to about 30 per cent. Levin<sup>65</sup> advocates radical operation for cases of malignancy followed by postoperative radiotherapy in every case of malignant tumor of the breast.

In cases of mammary carcinoma in the young, Lee<sup>66</sup> et al., emphasize the poor end results following radical surgical intervention, but few patients survive the three-year period.

Chealte and Cutler<sup>67</sup> give an excellent review of the literature of Paget's disease of the nipple with a report of the clinical and microscopic study of 17 breasts by means of whole serial sections. The authors are not convinced that the formation of "Paget's cells" and the early separation of the basal epidermal cells from each other are preliminary to malignant disease of these cells. (This is an important contribution on Paget's disease.)

#### GENITOURINARY SYSTEM

Chronic inflammation of the female urethra may be due to an infection of the tubular glands located around and opening into the posterior portion of the female urethra. Folsom<sup>68</sup> described these glands and also some adenomatous papillary structures which he classifies as inflammatory rather than neoplastic. Concretions found in the posterior urethra have an autochthonous development. According to Renner<sup>69</sup> only the rudimentary prostatic portions can be considered as being the site of origin of the small stones. The glands which have been found correspond morphologically to the male prostatic glands. The character and dilatability of ureteral fistulae are determined by cystoscopic examination. Ottow<sup>70</sup> has shown that fistulae of the ureter which lie in the wall of the bladder can be cured by insertion of a permanent catheter into the injured ureter.

About 50 cases of primary carcinoma of the ureter have been reported in the literature. Renner<sup>71</sup> describes a primary carcinosarcoma of the right ureter.

In a report of 40 cases of enuresis Thomas and Hubbell<sup>72</sup> give as the main etiologic factors: (a) pathology of the urinary organs; (b) disturbance of the reflex arc, and (c) disturbance of cerebral control. Walz<sup>73</sup> diagnosed a case of enuresis ureterica by means of retrograde and intravenous pyelography and the kolposcope. If the kidney and bladder are not too badly inflamed the extravasical opening of the ureter is treated by bladder implantation. Fifty-five of Natvig's<sup>74</sup> 63 cases of urinary incontinence were due to mechanical causes. The latter are successfully treated by one of three methods: (1) Bonner's tightening of the sub-urethral fascia in cases without prolapse; (2) the interposition operation; (3) a pyramidalis fascia plastic operation.

In cases of urinary incontinence due to loss or destruction of the urethra and vesicle sphincter, Douglass<sup>75</sup> reconstructs the urethra and utilizes the levator ani muscle as a sphincter. He reports three successful cases. Mashbitz<sup>76</sup> recommends the direct muscle reinforcement in addition to a perineal plastic in the treatment of cases of incontinence. In his 53 cases there was one recurrence on the twelfth day, and one death. Acute urinary retention is often mechanical in origin. Snodgrass<sup>77</sup> reports a case due to hematocolpometra.

The opinion that every action of the ureteral ostium in the bladder is the motor termination of a peristaltic wave which originates in the renal pelvis and passes along the ureter is not always correct. Ottow<sup>78</sup> believes that the bladder ostia of ureters without kidneys or ostia without ureters show similar action.

## EXTERNAL GENITALIA

Templeton, Stein and Schochet<sup>69</sup> note that spontaneous rhythmic contractions are present in the vagina of adult human females during the childbearing period and are absent in the menopause. These rhythmic contractions are most marked in the postmenstrual week and can not be induced or influenced by contractions from adjacent organs. (This important contribution is the first report in the literature dealing with the human species, and further studies should elucidate problems in frigidity and functional results of operative procedures. J. E. L.) Damm<sup>70</sup> reports a case of esthiomene of the vulva. He believes that the condition is caused by pathologic conditions of the regional lymph nodes leading to a local blocking of the lymph flow and lowering of the resistance of the tissues. It is due to a syphilitic infection and should be designated as syphiloma vulvae, according to A. Stein. Levin<sup>71</sup> describes ulcus vulvae acutum as a distinct entity appearing in three forms—gangrenous, venereal and malignant. It involves the labia majora and minora and is not infectious. Ulrich<sup>72</sup> points out that in the whole body economy only the stomach and the vagina supply acid secretions. Temporary or lasting hyperacidity of the vagina may be the cause of sterility. Baldwin<sup>73</sup> reports a case of primary carcinoma of the vagina in a girl fourteen years of age. Hinselman<sup>74</sup> advises the use of the kolposcope in examining cases of leukoplakia and carcinoma of the vagina. With a lens (in which there is a magnification of fourteen to forty) in the kolposcope he finds a condition which he calls "Felderung"<sup>75</sup> which accompanies leukoplakia and can only occur where cylindrical epithelium has been present. In this condition there is a filling of the abortive glands with epithelium or a filling of the ducts to the glands with epithelium.

Fels<sup>76</sup> was unable to produce experimental carcinoma by the application of tar to the vagina of the mouse. Less than one per cent of all carcinomas occur primarily in the vagina. At the Mayo Clinic from 1915 to 1925 there were 29 vaginal epitheliomas and 1246 cervical carcinomas—a ratio of one to forty-three. Two forms of early carcinoma occur, one simulates a benign papilloma (except for microscopic structure). The second form appears as a small firm nodule which later breaks down into an ulcer. Of the early cases treated with rays the average length of life was two years ten months and fifteen days. Of the early cases treated with surgery and radium the average duration of life was one year. With all methods of treatment Moench<sup>77</sup> reports a cure of 17 per cent. This deplorably low percentage indicates not only the high degree of malignancy but the failure of early diagnosis and ineffectiveness of our present methods of treatment.

Terwilliger<sup>78</sup> treated 42 infants with vulvovaginitis by means of gonococcal vaccine, and obtained a cure in 16 cases. Ivanov<sup>79</sup> made 200 biopsies in cases of acute or chronic vaginitis in which the specimens included the whole thickness of the vaginal wall. He found that the clinical phenomena may disappear and the mucosa appear normal while gonococci may still remain in the deeper layers. In acute gonorrheal vaginitis the infiltration hyperemia and other phenomena of inflammation frequently penetrate deeply into the muscle layer. (Experimentally this study of biopsy in vaginitis may be considered an excellent contribution.)

Monilia are frequently present in the vagina of patients suffering from vulvovaginitis and may be concerned with its etiology. Monilia vaginitis in pregnant women is a definite source of infection in sporadic outbreaks of oral thrush in the newborn as reported by Plass.<sup>80</sup>

Cornell<sup>81</sup> was able to grow trichomonas vaginalis in Lynch's media. Of 38 of these patients 12 showed symptoms of burning and profuse discharge.

Greenhill<sup>82</sup> procedure in the treatment of trichomonas vaginalis: thorough scrubbing of the vagina with tincture of green soap and water, then applying hexylresorcinol and inserting glycerine tampons. This is repeated every second day until two successive hanging drops are negative for trichomonas. Goodall<sup>84</sup> believes that vaginal cones of one per cent trinitrophenol inserted into the vagina each night act as a specific against trichomonas.

Goff<sup>85</sup> in a careful study of the pelvic floor could not demonstrate a true fascial plane in the walls of vagina, urethra, bladder and rectum. The muscular coat beneath the vaginal mucosa has been incorrectly called fascia. Bissell<sup>86</sup> in discussing the above article states that in 1929 he pointed out that the vaginal tissue used in the lapping technic for cure of cystocele was not fascia but muscle. W. Blair-Bell<sup>87</sup> calls attention to one of his publications in 1910, in which he described a uteropubic muscle layer derived from the internal muscle coat of the uterus. Bazala<sup>88</sup> describes three operations for artificial vagina, employing respectively the rectum, small intestine, and the sigmoid flexure. The first (Baldwin operation) has a high mortality with severe complications such as gangrene of the

intestine and ileus. The small intestine, when used as a vaginal canal in the Schubert operation, has a profuse irritating secretion which Stoeckel says can be controlled by diet. The use of the sigmoid flexure is more satisfactory because it is larger and more mobile, and the operation more easily performed. (Bazala.)

#### MENSTRUATION

There is convincing evidence from studies of the primate cycle that the theories of Bischoff and Meyer concerning the relation of menstruation to ovulation must be modified. Hartman<sup>89</sup> believes that menstruation begins with the Salachian fishes and that bleeding in the Mullerian derivatives is of widespread occurrence. The chief advances on the comparative side of menstruation have been made by zoologists among whom may be listed Heape and F. H. A. Marshall, and the American anatomists Corner, Hartman and Bartelmez. The size of the sella turcica in adolescent girls is related to the activity of the pelvic organs and the menstrual function.<sup>90</sup> Eufinger and Arntz<sup>91</sup> found that in 83.4 per cent of the 30 women studied, the sympathetic nervous system was affected by the menstrual cycle. Knaus<sup>92</sup> in a study of 25 patients with a 28 day menstrual cycle concluded that ovulation occurred 14 to 16 days before the onset of the flow. The obstetrical staff of the Kumamoto Imperial Medical College,<sup>93</sup> found that the shortest period of time between the first and second menstruation was a month, the longest four years and five months. In 92 per cent the average interval was from one to six months.

Hartman<sup>94</sup> et al. have shown that ovulation may be absent during long periods in which there is uterine bleeding. From their experiments it would seem to be possible to produce bleeding in a woman more readily than to stimulate a refractory ovary and hence a dormant uterus into action. The gynecologist must determine what benefit a patient receives from a mere bleeding without the usual concomitant estrous and particularly without the pregravid changes.

It has been shown in the higher monkeys that there may be periodic bleedings from the uterus without ovulation. Clinically these are indistinguishable from menstruation, but occur in the absence of large follicles of corpora lutea. The above observations were first described by Van Herwerden, but the conclusive evidence was first obtained by Corner.

Bartelmez<sup>95</sup> in a study of the human uterine mucous membrane during menstruation found that the entire spongy zone is not always lost. In specimens from the uteri of the first day of menstruation, gland cells show great variability in the degree of involution due to the fact that in some cases the stimulus to secretory activity from the ovary probably continues longer than in others. The control of the vascular apparatus is independent of the cyclic ovarian changes. Cessation of menstruation after complete ovariectomy may be explained as due to the insusceptibility of a mucous membrane which has become atrophic. Variability of function in different regions of the same mucous membrane occurs during menstruation as well as during other stages of the menstrual cycle. (This paper is one of the few well controlled studies of menstruation in gynecologic literature.)

From a study of the morphology of menstrual blood Geist<sup>96</sup> is able to identify the true menstrual discharge in about 90 per cent of the cases. This will frequently aid in the differential diagnosis between menstrual bleeding and the other types of hemorrhagic vaginal discharge. (An excellent contribution.)

#### CERVIX

Neisserian infection with its far-reaching ill effect on the health of the individual, its intractable course and its attendant complications is one of the most important chapters in gynecology. Gonorrhea of the cervix is characterized by periglandular infiltration of round and plasma cells. Schröder<sup>97</sup> finds small abscesses around the fundus of the glands. The glandular epithelium is frequently replaced by stratified pavement epithelium.

Missett<sup>98</sup> reports a case of primary tuberculosis of the cervix. According to Bonnet and Bulliard<sup>99</sup> the cervix is less frequently involved with primary tuberculosis than any other part of the female genital tract. Usually it is found in women with active or inactive tuberculous foci in the body. (In our autopsy experience we found uterine tuberculosis associated with pulmonary tuberculosis much more frequent than reported in the literature.)

The mucosa covering the portio is invaded by syphilis more often than that of the cervical canal. Involvement of the parenchyma of the cervix is extremely rare. The lesions tend to become progressive until the entire vagina and uterus are affected. In an analysis of material at the Rivadavia Hospital, Puente<sup>100</sup> found 29 cases of chancre, 28 cases of secondary syphilis and three cases of leukoplakia of the

cervix. Chancre of the cervix does not cause symptoms, is of short duration and heals rapidly. Secondary syphilis of the cervix is generally thought to be very rare. The author found 29 among 222 cases of secondary syphilis (13 per cent). (The findings of secondary syphilitic involvement of the cervix do not tally with the reports of other clinics. The late Professor Warthin informed one of us that he observed only one case of secondary lues of the cervical endometrium in his extensive studies of syphilis.)

Whatever operative procedure is applied to the cervical area whether it be actual cautery, radium or Sturmdorf's cone excision, the complete destruction of infected racemose glands in the cervix is of paramount importance for the cure of the lesion. Holden<sup>101</sup> in a review of 500 case records gives the following contraindications to cervical cauterization: (1) where the disorder is one of several requiring operation; (2) slight inflammation without eversion or erosion; (3) simple edemas; and (4) those that do better with other treatment after trial of cautery. (We do not think that group four should be classified as a contraindication to cauterization when once attempted as a means of cure.) The treatment of cystic endocervicitis with electrocoagulation is equally as good as the Sturmdorf operation. Roblee<sup>101</sup> found no cases complicated by stenosis.

Thermocautery is preferred to electrocoagulation in cases of recent postpartum laceration where it is advisable to destroy the cervical tissue to the point of retraction. It is also to be preferred in recent postpartum erosions and recent postpartum endocervicitis. (In these cases the infection is usually superficial and is cured with silver nitrate or left to normal involution.)

In the chronic cervicitis group electrocoagulation is preferable. Roblee<sup>101</sup> however advises the combination of both methods in an endeavor to obtain the best results. Brown<sup>102</sup> prefers the Sturmdorf operation in cases showing extensive hyperplasia and cyst formation either with or without tears. Offut<sup>103</sup> points out three possible complications of cervical cauterization, namely, hemorrhage, stenosis and pelvic infection.

Rogge<sup>104</sup> states that the kolposcope is the only real method of early diagnosis of precancerous leukoplakia of the portio. (The kolposcope is a definite contribution to the gynecologic armamentarium. However, we should not lose sight of the fact that biopsy is a perfected and time honored method and is not an obsolete procedure for the early diagnosis of malignancy.) Schneider<sup>105</sup> recommends the use of the metranokter for dilating the cervix when digital examination of the cervical canal is also indicated. (We prefer vaginal hysterotomy for this group of cases.)

#### UTERUS

The vascular system of the female sex apparatus plays a more important rôle in health and disease than gynecologists generally attribute to it. Polak and Mazzola<sup>106</sup> in a study of the effects of experimental torsion of the uterus on the vessels of the parametrium and contiguous tissues show, that displacements cause an increase both in the size of the uterus and in the number and size of the blood vessels. Interference with venous flow in the pelvis often causes varicosities in the absence of infection. (This is an important problem which has not received the attention that it deserves.)

Magid<sup>107</sup> in a study of 500 cases finds that there are certain types of women who present anatomic relations between spine and pelvis that are at variance with the norm and that the uteri in this group assume a position which is essential or normal to these types of women. Any attempt to correct these variations of position in this group of cases with the hope of relieving symptoms will result in failure. Agaronow<sup>108</sup> believes that myomas of the uterus develop as the result of hyperfunction of the ovary. Since the ovary and hypophysis influence the basal metabolic rate he urges a careful study of basal metabolism in the various disorders of the genital sphere. The studies of Vassitch confirm the belief in the frequent coexistence of uterine fibromas and arterial hypertension. He is of the opinion that the action of the fibromas in arterial tension is mechanical. Their frequent coexistence should be considered as an evolutionary coincidence.

Parfenoff<sup>109</sup> demonstrates degenerative changes in the ovary (especially in the follicle) of white mice following extirpation of the uterus. Removal of the uterus stimulates the formation of the interstitial gland which causes the atrophy of the follicle. Archer and Greenberg<sup>111</sup> present a case of floating uterus. Fluhmann and Morse<sup>112</sup> analyzed 1137 consecutive cases of abnormal uterine bleeding. They subdivided them into two groups as suggested by Cullen (1) hemorrhages associated with pregnancy and (2) hemorrhages in the non-pregnant. This report includes 507 hemorrhages in the non-pregnant state which are subdivided into: (1) menorrhagias in patients

with otherwise normal menses; (2) an irregularity in the menses due to disturbance of ovarian function of endocrine origin; (3) hemorrhages initiated with a menstrual period, that may be prolonged, with a lesion of the endometrium; (4) hemorrhages in the middle of the menstrual cycle caused by the rupture of the graafian follicle; (5) hemorrhages due to hyperplasia of the endometrium; (6) bleeding that follows amenorrhea due to hyperplasia of endometrium which follows ovariectomy; (7) patients with atypical irregular bleeding having no definite relation to the menstrual cycle, and (8) bleeding following menopause. Martin<sup>123</sup> asserts that chronic uterine hemorrhage without demonstrable pelvic pathologic changes is a common condition and that the etiologic factor is some abnormality of the endocrine system. Smith<sup>124</sup> believes that it is important to consider the question of allergy in all cases of essential dysmenorrhea. With the exception of a recent childbed or gonorrhoeic infection, Young<sup>125</sup> finds that inflammations of the endometrium or myometrium are rarely the cause of irregular and excessive uterine hemorrhages.

Brown<sup>126</sup> reports an unusual involvement of the uterus with tuberculosis. The process extended directly from the tubes to the myometrium with no apparent intervening involvement of the endometrium. (In this case it appears to us that the endometrium was most probably primarily involved, but that the existing endometrial port of entrance healed or was removed by the normal destruction which occurs during menstruation.)

Holden<sup>127</sup> describes a case of adenomyoma of the uterus in a girl fourteen years of age. De Gaetano<sup>128</sup> noted that uterine myofibromas develop more commonly in women of somewhat masculine appearance with a brown complexion, robust, full-blooded with down on the upper lip, chin, over the linea alba and on the limbs. They have a tendency to obesity with an exaggerated libido and leaning toward their own sex.

Uterine hemorrhages cause a salutary effect on the stasis of the inferior caval system. Lebon and Laffont<sup>129</sup> report a case of uterine bleeding due to mitral stenosis.

Nurnberger<sup>130</sup> emphasizes the importance of the pathologically increased elimination of substances in the urine, in cases of hydatid mole and chorion-

epithelioma. (It is difficult to determine accurately this increase of anterior pituitary hormone on biologic assay.) Bompiani and Martinotti<sup>131</sup> advise a hysterectomy in hydatid mole for grave hemorrhage, anemia, and in those cases in which chorionepithelioma is suspected.

Leiomyosarcomas of the uterus are found in one per cent of all myomatous uteri examined. Meaker<sup>132</sup> describes four cases, one of which was a true myoma malignum. Although only a small portion prove to be clinically malignant, all leiomyosarcomas must be treated as potentially malignant with a radical operation followed by x-rays.

Schmitz<sup>133</sup> reviews eight cases of malignant and three cases of benign choriomas. The persistence of chorionic connective tissue of the villi with proliferation is characteristic of the benign choriomas. Absence of connective tissue with an aplasia and atypia of the chorionic epithelium is characteristic of the malignant type. (We find it often very difficult to make a diagnosis of chorioma malignum from microscopic slides.) Roentgen-ray examination and the Aschheim-Zondek pregnancy reaction may be of value in the diagnosis of a malignant chorioma. Hysterectomy followed by radiation lessens the number of recurrences.

Fluhmann<sup>134</sup> considers hyperplasia of the endometrium to be part of a definite clinicopathological entity. It was found in 2.8 per cent of 1700 patients admitted to the gynecologic service of the Stanford Hospital, and in 12.2 per cent of 507 women with abnormal uterine hemorrhage. Bleeding is the most constant symptom. Functional studies have demonstrated an excessive production of the female sex hormone.

The cause of endometrial hyperplasia is still inadequately understood. Many workers believe that an unrecognized endocrine factor is concerned in its etiology. According to Hofbauer<sup>135</sup> it may reasonably be regarded as the manifestation of an overactivity of the anterior pituitary lobe. This view is corroborated by the clinical experience that the condition commonly recurs after repeated curettage.

Neumann<sup>136</sup> reports a case with increase in the lymph follicles of the endometrium, probably a part of a picture of status lymphaticus. (From the reports of many anatomists it appears doubtful that lymphatics are present in the endometrium.)

Menstrual molimina in a rudimentary uterus have a psychosexual etiology. In this type of case, Kehrer<sup>137</sup> states, operation is useless.

Hirsch-Hoffman<sup>138</sup> concur in the accepted belief that primary amenorrheas of young girls with hypoplastic genitalia, and secondary amenorrheas following abortion or confinement react best under hypophyseal hormone therapy. Novak and Hurd<sup>139</sup> treated 51 cases of functional uterine hemorrhage with an anterior pituitary luteinizing principle derived from the urine of pregnant women. In 44 cases they

successfully checked the abnormal bleeding. The characteristic anatomic finding is an absence of corpora lutea. (This is an important contribution to the study of functional bleedings.)

When there is considerable inflammation of the adnexa with a fixed retroverted uterus, Werner<sup>130</sup> performs a vaginal hysterectomy in which the uterus first is split and each half is extirpated with the adnexa, beginning with the side which is less difficult to remove. (It seems to us that the abdominal route is preferable in this group of cases.)

In women under 41 years of age, myomectomy is the operation of choice. Bonney<sup>131</sup> has performed myomectomy 403 times with an operative mortality of 1.7 per cent. In single instances he has removed from 15 to 125 myomas. In 3 per cent of his cases he subsequently performed a hysterectomy for recurrent fibroids or for hemorrhage. Of the women of childbearing age who were subjected to myomectomy 39 per cent later became pregnant. The operation should not be performed unless the uterus apart from its contained fibroids is reasonably healthy, and malignancy is not suspected. Consoli and Allesandri<sup>132</sup> regard myomectomy as an operation destined to be more widely used in dealing with women during the childbearing age. Cova<sup>132</sup> in 1000 laparotomies performed a hysterectomy 202 times and myomectomy 16 times. (As a rule, the postoperative course in myomectomy is more stormy than in hysterectomy.)

Burch and Burch<sup>133</sup> report nine deaths in a series of 200 consecutive hysterectomies, a mortality of 4.5 per cent. They stress the danger of hemorrhage under spinal anesthesia and condemn the use of zinc chloride as an agent for chemical hysterectomy. (This high mortality is most probably due to other causes than the operative procedure.)

Howard Kelly<sup>134</sup> says that x-ray is practically a specific in menopausal hemorrhage. Koenig<sup>135</sup> used radium therapy in 85 cases of noncancerous diseases of the uterus with excellent endresults. Corsecaden<sup>136</sup> was able to follow up 393 of 434 women treated with rays for benign uterine conditions. The average follow-up was seven years. He found that radiation is a safe method. A reduction in the size of the fibromyoma occurred in 96 per cent. There was a complete disappearance in 55.2 per cent; the uterus was reduced nearly one half in size, in 28.3 per cent, and a definite but unimportant reduction occurred in 12 per cent. Van Dongen<sup>137</sup> prefers operation to x-ray in the treatment of myomas on account of the menopausal symptoms due to radiation. (We believe that surgery is preferable.)

#### MALPOSITIONS AND DISPLACEMENTS

In spite of the apparent frequency of ureteral dilatation in cases of prolapse of the uterus, serious bladder and kidney symptoms ascribed to this cause have rarely been reported. Robert Frank<sup>138</sup> has found only two cases in the literature in which there was a fatal outcome. He reports a case of complete prolapse of the uterus with bilateral pyonephrosis, extreme bilateral hydroureter and dilatation of the ureters.

Marondis<sup>139</sup> describes a case of complete genital prolapse in a baby with aplasia of the pelvic floor. There was no evidence of associated spina bifida or bony maldevelopment of the pelvis.

Meshberg<sup>140</sup> discusses 128 interposition operations for prolapse. As a rule amputation of the cervix, perineorrhaphy, ligation of the tubes, plication of the vesical sphincter and curettage were performed with the interposition. Cystitis was the most troublesome complication. Ninety-two patients were traced. Among them were six operative failures (6.5 per cent), and seven symptomatic failures. (It should be borne in mind that the average failure of all forms of operations for prolapse of the uterus among different surgeons is reported as 10 to 12 per cent.)

Rongy<sup>141</sup> favors the vaginal fixation operation. Properly executed in selected cases it will cure the largest number of patients. One of the commonest criticisms of this operation is that so many patients complain of bladder disturbances. Graves and Smith<sup>142</sup> review 3358 cases operated upon for suspension of the uterus by Olshausen's method. The defects in this operation are postoperative sinus, intestinal obstruction (which occurred in six cases), and hernia at the site of the suspending ligature. Of the total number 17.2 per cent were not traced; 66.8 per cent were cured symptomatically; 27.3 per cent were relieved; failure occurred in 5.6 per cent. In 76.9 per cent of the cases the uterus was found in good position. There was complete recurrence in 8.8 per cent, and partial recurrence in 14.2 per cent. Westman<sup>143</sup> reports 69 cases of interposition operation with colpoperineorrhaphy with a primary operative mortality of 4.3 per cent. Of 61 patients followed up 85.2 per cent were free from symptoms; 6.6 had slight and 8.2 per cent considerable discomfort.



Lagerson<sup>144</sup> describes a modification of the Webster-Baldy operation in which the round ligament is attached to the posterior wall of the uterus after pulling it through the subserous tissues, thus causing better adhesion and firmer suspension. (In our service we prefer vaginal hysterectomy for prolapse.)

#### MALIGNANCY

As a result of the apparent increase in the number of cancer patients and the comparatively poor results of treatment—due to late diagnosis, there exists a continuous movement toward greater and greater specialization in the cancer field. Lombard<sup>145</sup> states that less than two per cent of the cancer patients in Delaware report early enough for successful treatment. The figures for certain cancer hospitals in Philadelphia and New York City are 4.2 per cent and 25 per cent respectively for operability.

Our only hope to combat this deplorable state of conditions lies (1) in the establishment of cancer centers with well organized institutes and tumor clinics; (2) education of the general medical profession in the early recognition of malignancy and (3) propaganda for a routine periodic examination among the lay public.

A cancer institute according to James Ewing,<sup>146</sup> the world's foremost authority on neoplasms, should consist of cancer hospitals with large clinical material, well trained staff of specialists in the clinical branches with special equipment and specialists in departments of radiobiology, radiophysiology, radiotherapy, biochemistry, biophysics, general biology, genetics and pathology. The pathologist must be well trained and highly specialized in tumor pathology. An institute of this type requires money. Ewing is of the opinion that it is of questionable wisdom to attempt to establish a cancer institute with an endowment of less than ten million dollars. The tumor clinics of the general hospital are purely diagnostic with limited means for therapeutic treatment. They are great aids in combating malignancy provided they recognize their limitations and do not prostitute the true meaning of a cancer hospital. At present there are 40 cancer diagnostic clinics<sup>147</sup> in the United States but their rôle will have limited effect in reducing the rising incidence and death rate from cancer.

Bloodgood<sup>148, 149</sup> finds that more ample provision for physicians to become proficient in the diagnosis of precancerous and early stages of cancer is needed. Von Franqué<sup>150</sup> cites Winter as reporting that procrastination in the treatment of carcinoma in patients under his care during the period from 1911 to 1920 could be attributed to physicians in 21.5 per cent of the cases, to midwives in 3.4, to quacks in 0.6 per cent and to the women themselves through ignorance and carelessness in 74.5 per cent.

Occasionally complications result from biopsies, but Epstein and Fedorejeff<sup>151</sup> find that the percentage of these cases to the total number of biopsies is insignificant. There is only an apparent immunity against cancer in complete procidentia, although Delvaux<sup>152</sup> states he has never observed cervical carcinoma in cases of complete prolapse. Hofbauer<sup>153</sup> describes metaplastic changes of the cell character, and displacements of the epithelial connective tissue line in the cervix during pregnancy. He assumes that these changes may be of etiologic significance for the development of malignant growths. In an analysis of tumor resistance, Waterman<sup>154</sup> finds that the cancer cell is the product of fermentative degeneration, and that injection of spleen extracts induces tumor cell resistance. This view in part is confirmed by Edelmann, Schönbauer and Schloss<sup>155</sup> who find that autolysates from fresh carcinomas dissolve carcinoma cells. In the twenty-ninth annual report<sup>156</sup> of the Imperial Cancer Research Fund, many striking examples are mentioned of cases in which tumor cells proved more resistant to radium than normal cells. It is a known fact that there are individuals who are especially sensitive to radium.<sup>157</sup> Martland<sup>158, 159</sup> from his extensive studies on workers in radioactive products suggests that certain conditions (bone sarcomas) may depend on the presence in the human body of increased amounts of radioactive substances. The sale of all radioactive waters, emanators, activators, etc., should be under Federal control.<sup>160</sup> Crile<sup>161</sup> thinks that cancer owes its development to some alteration in the cells of the tissues as a result of some mechanical, physical or chemical factor. (Suggestions without proof do not materially aid in the solution of the cancer problem.)

Maud Slye<sup>162</sup> reports a very interesting group of records of an entire single strain of mice from mating of a cancerous female and noncancerous male and bred through three generations. There were 11 per cent of cancerous offspring which closely approximates the percentage of occurrence of neoplasm in man.

Hinselman<sup>163</sup> has given us a valuable instrument—the kolposcope for the diagnosis of leukoplakia.

Three interesting cases of primary vaginal carcinoma are cited in this year's literature. Wolfe's<sup>164</sup> case due to irritation from a pessary; Gragert's<sup>165</sup> case of choristoblastoma from the vagina with probable origin from elements of the rectal mucosa; and Baldwin's<sup>166</sup> report of a primary carcinoma of the vagina in a girl of fourteen. The endresults of the treatment of primary vaginal carcinoma are not encouraging. Buben<sup>167</sup> employs x-ray and radium. Of 28 patients reported nine are living although only two of them can be regarded as cured. Heyman reports two recoveries in 16 patients treated with radium at the Royal Institute of Stockholm.

A large percentage of cancer cases seen in clinics is so far advanced that the diagnosis is obvious. This may be due to the fact that the early diagnosis is difficult and not necessarily due to gross ignorance of the general practitioner. Schneider<sup>168</sup> finds that the miostagmin reaction is of diagnostic value and is useful in determining the prognosis of many cases in regard to radium treatment. Hoehne<sup>169</sup> reports an increase in the cholesterolin in blood serum of carcinomatous patients after x-ray treatment which is absent in cancer-free patients. (In spite of these valuable laboratory aids the importance of clinical symptoms must not be overlooked.) Whitehouse<sup>170</sup> states that in 30 per cent of all women who suffer from cancer the organ first involved is the uterus. The earliest and most important symptom of carcinoma affecting the uterus, whether it be cervix or corpus, is almost invariably hemorrhage.

MacCarty<sup>171</sup> believes that it is a grave mistake with present knowledge to use any one criterion as the basis of clinical prognosis in cancer. The mere microscopic grading of cancer is not of great clinical value when the other fifteen or more factors governing prognosis are not considered. Döderlein<sup>172</sup> finds that adenocarcinoma of the cervix has the most unfavorable prognosis irrespective of the degree of maturity of the cancer cells. The histologic character of cervical carcinoma is of importance only in so far as adenomatous cancers yield to irradiation much less readily than solid carcinomas. Taylor<sup>173</sup> presents a clinical and pathologic study of 739 cases of gynecologic cancer observed at the Roosevelt Hospital. In 1921-1923 the plan of treatment for favorable cases was preoperative radium and later radical hysterectomy; the absolute five year cure rate was 29.7 per cent. A careful review has led to little corroboration of the claim of several writers that histologic form bears a relation to prognosis as the result of variations in malignancy or in radiosensitivity.

There is a small group of inoperable cases of cancer reported from unquestionable sources that have been cured merely by palliative means.<sup>174, 175</sup>

The Mayos<sup>176</sup> found in their records 99 cervical stump carcinomas. Of this number 12 had been previously operated for benign conditions in their clinic and 23 in other hospitals. The authors believe that a lower incidence of stump carcinoma results from their routine of coning out the cervix in all cases of subtotal hysterectomy.

Primary carcinoma of the fallopian tubes according to Stubler and Brandes represents 0.45 per cent of all genital cancers. An approximate idea of its rareness is conveyed by the fact that it occurred but once in 19432 gynecologic cases at the University Hospital in Philadelphia; five times in 35000 cases at Johns Hopkins Hospital; and three times in 30000 at the Bellevue Hospital. About 234 cases have been reported in the literature since Orthmann's first description of primary carcinoma of the tubes. During the past year, Anspach and Hoffman<sup>177</sup> recorded two additional cases; Rabinovitch and Horton<sup>178</sup>; Johnson<sup>179</sup> and Hunter and Holden<sup>180</sup> each one case.

Ovarian carcinomas are not rare. They differ from other neoplasms in their histogenesis, character, and radiosensitivity. According to Monlonguet and Mallet<sup>181</sup> the sarcomas are more radiosensitive than the epitheliomas. Metastasis to the thyroid gland is rare although Wegelin has frequently found it present. Hoffman<sup>182</sup> records a case of carcinoma of the ovary with metastases in the thyroid gland and with Basedow's syndrome.

Anspach and Hoffman<sup>183</sup> look upon chorionepithelioma of the uterus in a certain sense as a physiologic process overstepping its normal bounds. An atypical case is described in which free intraperitoneal hemorrhage occurred due to perforation of the uterine wall. Although most authors recommend surgical treatment for chorionepithelioma, Wintz<sup>184</sup> reports eleven cases in which he employed irradiation. He has found that these malignant cells are from 40 to 50 per cent more sensitive to rays than the cells of the surrounding normal tissues. Of this group, 8 patients are still alive.

A cross-section study of the published reports of treatment of carcinoma of the cervix and uterus strongly suggests that equally good results may be obtained with radiotherapy as with surgical procedures. It must be borne in mind, however, that

these results are obtained only by those workers who are thoroughly trained in radium therapy. If the dosage is suitable for a certain case, the cancer cells but not the normal tissues are destroyed. If the cancer cells are radiated insufficiently they become radioresistant. Ward and Farrar<sup>185</sup> are of the opinion that this danger occurs only when prolonged applications of heavy dosage are used and when they are repeated at too frequent intervals. Of 170 of their cases of epidermoid and adenocarcinoma of the cervix, 50 per cent had more than one radium treatment and 26.5 per cent of all radiated patients lived five years or more. Lynch<sup>186</sup> reviewed 192 cervical cancers of a five to fifteen year period and found that nearly one-fourth of the five year survivors died subsequently from recurrence of their original cancer or developed other cancers of equal importance. Crossen's<sup>187</sup> series of 121 cases of five year cures consisted of 108 squamous cell carcinomata and 13 adenocarcinomata. Classified clinically there were two in Group I; one in Group II; 108 in Group III; and ten cases in Group IV. The two patients in Group I were operated without radiation and survived eight and nine years. Of the 108 patients in Group III, 24 survived for five years and 21 of the latter are still living, some as long as eight years after treatment. Of the 10 patients in Group IV not one survived five years. The author emphasizes that the time to cure cancer with greatest certainty is before it starts. In a review of 325 cases of carcinoma of the cervix Jones<sup>188</sup> believes that surgery is excellent treatment for early cases but that irradiation will cure as many of the early cases as will surgery without any mortality or morbidity.

Healy<sup>189</sup> analyzes 1574 cases of cervical cancer. Histologically 97.3 per cent of the cases were squamous epidermoid carcinomas and 2.7 per cent adenocarcinomas. Only from 20 to 22 per cent of all patients treated survive five years, regardless of the method of treatment employed.

It is difficult to correlate statistics from various sources because of the great personal equation that enters into the classification of patients according to the clinical stage of the growth. Neef<sup>190</sup> feels that as a fair average it might be said in round numbers that the five year cures which have been obtained by radiotherapy amount to about 36 per cent in operable, 26 per cent in borderline, and 16 per cent in advanced cases. Similar endresults in large series were reported by Scheffey,<sup>191</sup> Bartlett,<sup>192</sup> Dailey<sup>193</sup> (age incidence) Held,<sup>194</sup> and Povey.<sup>195</sup>

The operative mortality of the Wertheim operation in 407 cases reported by Bonney<sup>196</sup> was 14 per cent, but in the last 100 of his cases it was only 6 per cent. The Schauta-Stoeckel vaginal operation for cancer of the cervix is described in detail by Maluschew.<sup>197</sup> Stoeckel<sup>198</sup> is convinced that with his vaginal operation one can remove more of the parametrium and that there is less bleeding. Three or four weeks after the operation deep x-ray treatments are given. Mosquot and Boquel<sup>199</sup> discuss the end results of their 65 cases in which hysterectomy was performed by the combined vaginobdominal route. In this series the operative mortality was 9.23 per cent.

(A cross-section study of the endresults of treatment of carcinoma of the cervix with irradiation, with surgery alone, or surgery followed by irradiation convinces us that the ideal method of treatment has not been found.)

#### ENDOMETRIOSIS

We are indebted to Sampson for presenting a most comprehensive study of endometriomata and for focusing attention upon the frequency of this condition. In well controlled experimental studies, Schochet, Allen and Bauer, have conclusively shown that endometrial transplants in the anterior chambers of the eye grow for long periods of time and undergo marked hyperplasia. Everette<sup>200</sup> confirms Sampson's studies on tubal endometriosis and finds strong evidence that tubal epithelium by metaplasia may give rise to endometriomata. Behring<sup>201</sup> believes that these hyperplastic changes or so-called endometriomata may be due to disturbances of the female sex hormone. In a careful survey of endometriomata King<sup>202</sup> concludes that the ductless glands play a greater rôle in the etiology than accepted, and that Sampson's theory of implantation should receive further study. Derichsweiler<sup>203</sup> discusses the etiology of endometriosis but offers little additional data except an extensive classification. Many interesting cases of endometriomata are reported with new groups of symptoms. Schuler<sup>204</sup> cites a case of ileus due to endometriosis of the intestine; Thompson<sup>205</sup> presents a careful study of endometriosis of the umbilicus; and Marcus<sup>206</sup> discusses endometriosis of the round ligament. Novak<sup>207</sup> describes three cases of rupture of endometrial cysts with clinical symptoms of a twisted ovarian cyst in one and of acute appendicitis in the other two cases.

## ABORTION

There occurs one abortion to three deliveries. Taussig<sup>205, 209</sup> emphasizes the fact that the death rate of abortions is seven times greater than that of full term childbirth. Reports from Russia show that the routine performance of legalized abortion, as a hospital procedure under aseptic precautions, has caused a marked decline in the maternal death rate. At Moscow (in 1926) 29,306 legalized abortions were performed without a reported death. In 2366 secretly performed abortions there were 35 deaths.

The maternal deaths are estimated as 15,000 in the approximately 700,000 criminal abortions annually performed in the United States. In a survey, by the Austrian Public Health Service, of 9000 abortions, pathologic sequelae developed in 9.6 per cent with a mortality of 0.75 per cent. There were two women who had fifteen abortions, and one who had sixteen!

Agaroun<sup>210</sup> reports five cases in which foreign bodies were left in the uterus in the attempt at abortion. Metzler<sup>211</sup> is in accord with the present day conservative treatment of abortion. Heine<sup>212</sup> recommends the use of perkain as a parametrial local anesthetic for emptying the uterus for a diagnostic curettage.

## ECTOPIC PREGNANCY

Of the many possible etiologic factors of extrauterine pregnancy, inflammatory lesions of the adnexa or adjacent organs are the more important. Desjardius<sup>213</sup> finds that radiotherapy is a most valuable adjunct in the treatment of acute, subacute and chronic inflammatory processes and that this method has not received the attention it deserves. (We are of the opinion that x-rays destroy the protective ferments and immune bodies.) The diagnosis of ectopic pregnancy in many instances is very difficult. Wladika<sup>214</sup> points out the great value of the Aschheim-Zondek test in the diagnosis of ectopic pregnancy and hydatid mole. Szello<sup>215</sup> cites two cases of intraligamentary pregnancy proved by roentgenoscopy (negative x-ray findings do not always exclude ectopic pregnancy); d'Allaines and Doubrere<sup>216</sup> describe the extrusion of fetal parts of a tubal pregnancy via the intestinal tract.

Müller and Oberling<sup>217</sup> report an increase in the number of cases of ectopic pregnancy for the period from 1925 to 1930 which parallels the increase in gonorrhea. A valuable aid in the diagnosis of ectopic pregnancy is locating a peritoneal inundation, a piercing pain in the culdesac on deep palpation. Contrary to these findings, Van Etten<sup>218</sup> points out that only 10.4 per cent of his 77 cases showed evidence of pre-existing inflammation. Ricci and DePalma<sup>219</sup> analyzed 100 cases of ruptured extrauterine pregnancy with profuse bleeding. There were 11 errors in diagnosis. In 16 cases there was no sudden lancinating pain and syncope. The authors employed autohemofusion in 11 cases. (We cite these papers to indicate that there still exists a marked divergence of opinion as to the rôle infection plays in the causation of extrauterine pregnancy.)

In 1878 Spiegelberg formulated certain criteria to be fulfilled before cases may be accepted as true ovarian pregnancy: (1) the tube on the affected side is intact, (2) the fetal sac occupies the position of the ovary, (3) this sac is connected with the uterus by the ovarian ligament and (4) ovarian tissue is found in its wall.

In 1906, Williams described 13 authentic cases of ovarian pregnancy, and in Lewis' System of Surgery 45 cases of ovarian pregnancy are accepted as authentic. Cramer's<sup>220</sup> case of ovarian pregnancy fulfills Spiegelberg's formula.

## STERILITY

The study of sterility in the female requires a more thorough understanding of the physiology and pathology of the generative system and associated organs than any other gynecologic condition. Mazer and Andrusier<sup>221</sup> maintain that ovarian function is dependent on hormonal stimulation from the pituitary gland. The test of Frank and Goldberger for the blood level of female sex hormone is of great value in the diagnosis of functional sterility in regularly menstruating women but is of little value when associated with menstrual disorders. The recovery of a demonstrable quantity of anterior pituitary sex hormone from the blood of women suffering from functional sterility is pathognomonic of primary ovarian failure. Low dosage irradiation of the affected endocrine glands was successful in reestablishing menstrual periodicity in more than 50 per cent of 38 women thus treated.

Knaus<sup>222</sup> estimates that fertilization occurs at the time of the termination of the process of ovulation. In a healthy woman who menstruates every twenty-eight days, ovulation takes place between the fourteenth and sixteenth day of the menstrual

cycle and the conception capacity is limited to the time between the eleventh and seventeenth day.

Bjorkenheim<sup>223</sup> reviews a series of 524 cases of sterility of which 424 were of the primary and 100 of the secondary type. Included are only patients sterile after three years of marriage. The most common etiologic factor was an inflammatory change in the adnexa and parametrium present in 35 per cent of the cases. Of 417 cases treated nine required surgical intervention. According to Newell<sup>224</sup> sterility occurs more commonly after puerperal than after gonorrheal infections. Moench and Holt<sup>225</sup> believe that the sperm head is the greatest single source of information as to the fitness of the male cell for reproduction. In the average cases the relative number of the abnormal sperm heads affords an index to reproductive fitness of the male. They found that a normal specimen of semen contains 19 to 20 per cent of abnormal sperm heads. If this number increases to from 20 to 23 per cent impaired fertility can be assumed. Schultze<sup>226</sup> suggests contrast visualization of the female genitalia as a complement to the other diagnostic methods of sterility. Smith<sup>227</sup> employs the combination of iodized oil and pneumoperitoneum, and believes it to yield the maximum information regarding the pelvic organs. It is surpassed only by exploratory laparotomy.

Turco<sup>228</sup> reports four cases in which surgical implantation of the tube was followed by tubal patency. In two cases the patients became pregnant and delivered at term.

Montag<sup>229</sup> recommends prolan as an aid in the treatment of sterility due to tubal infection. Naujoks<sup>230</sup> for temporary sterilization crushes and ligates the ampulla. Later if desired a salpingostomy can be performed. Haberland<sup>231</sup> discusses the possibility of producing temporary sterility by injection of hormones from ovary and placenta. (In the present state of knowledge concerning hormones, therapeutics should be more conservative.)

#### FALLOPIAN TUBES

Robins and Shapira<sup>232</sup> conclude from their experience with 1000 cases of hysterosalpingography that the dangers of tubal injections are infection, rupture of tube or uterus, extravasation of lipiodol into the blood vessels and abortions. This method is contraindicated in frank infections of any part of the genital tract, in hemorrhage, in pregnancy, in the presence of fever. Novak<sup>234</sup> cites a case in which it was necessary to remove the contrast material fifteen months after the injection. Gajzago<sup>235</sup> describes a death following the injection of iodized oil. Dutailles<sup>236</sup> shows the value of hysterosalpingography in the diagnosis of spasmodic obstructions of the fallopian tubes, and peritubal and periuterine adhesions. Markoff<sup>237</sup> inflated the tubes in a series of fetuses and found that in numerous instances the tubes were impermeable. He believes that many sterile women have a congenital impermeability of the tubes which is the cause of permanent sterility.

Baldwin<sup>238</sup> describes an instrument that will serve equally as well for the Rubin tests, injections of opaque media and pneumoperitoneum. The differential diagnosis between appendicitis and salpingitis is difficult. Polak states that appendectomy has been erroneously performed in 10 to 15 per cent of cases where tubal disease is the existing pathology. Rieci<sup>239</sup> emphasizes the importance of disturbed menstruation in the diagnosis of salpingitis. Fluhmann<sup>240</sup> finds abnormal uterine bleeding in 35 to 50 per cent of all patients suffering from acute or chronic salpingitis. The important factors concerned in the production of bleeding are (a) interference with uterine contractions from adhesions and malpositions, (b) pelvic hyperemia, (c) endometritis, (d) ovarian deficiency and (e) corpus luteum abscess formation.

Carlisle<sup>241</sup> in a series of 602 patients with pelvic inflammatory disease reports abnormal uterine bleeding in 40 per cent. According to Ivanov<sup>242</sup> the paravaginal lymphatic plexus is an important route in the extension of infections involving the internal female genitalia. Bearnse<sup>243</sup> corroborates Curtis's observation of flimsy cobweb-like perihepatic adhesions in a case of gonorrheal salpingitis three weeks after the onset of the disease. Downer and Brines<sup>244</sup> operated on a seven-year-old girl and found a torsion of the left adnexa with no apparent tuboovarian disease. This is the nineteenth reported case in the literature. Fainseiber and Portret<sup>245</sup> use diathermy in the conservative treatment of chronic salpingitis and report cures in 53 of 56 cases. Gellhorn<sup>246</sup> warns against the use of diathermy in acute and early subacute cases of salpingitis. The principle field of diathermy in gynecology is in the treatment of chronic pelvic infections.

Holden and Gurnee<sup>246</sup> recommend the Elliot treatment in acute salpingitis because it causes a more rapid absorption of the pathologic exudate. This is due to the fact

that a consistently uniform temperature of 130 degrees can be maintained for any length of time against the large area of distended vagina, cervix, parametrium and pelvic organs. Of 5233 treatments with the Elliot apparatus in 500 cases at the Bellevue Hospital there were one severe burn, eight mild burns in the lateral fornices, and eleven slight burns about the introitus. This method causes a more rapid resolution in shorter periods of time than any of the other methods of treatment.

Crainicianu and Pavelescu<sup>247</sup> applied regional vaccine therapy at the primary focus (Skene's ducts) in acute and subacute infections of the genital tract and report considerable success. (This study requires corroboration.) Douglas and Shelden<sup>248</sup> advocate the extraperitoneal surgical drainage of parametric exudates (the method of Cullen) for it shortens the convalescence and lessens the morbidity.

#### FEMALE SEX HORMONE AND OVARY

It is estimated that there are more than 3000 papers published annually on the glands of internal secretions. During the past few years there has been disproportionately larger activity in the study of the female sex hormone by anatomists, biochemists, physiologists and gynecologists with the result that many new "chemical messengers" have been partially isolated. Robert T. Frank<sup>249</sup> rightly states that when one analyzes the sex physiology in the female, it is necessary for one to consider all these chemical messengers or hormones. (This contribution on the rôle of the female sex hormone throws much light on many of our clinical problems.) Allen<sup>250</sup> discusses the endocrine activity of the ovary with special reference to the recent work on follicular and corpus luteum hormones and outlines the present conception of the factors responsible for the periodic changes in the genital organs during the menstrual cycle. The outstanding animal reaction to follicular hormone, "theelin" is growth of the accessory genital tissues. The same rules for the standardization of aqueous and oily solutions of hormones can not be applied to both. Dodds<sup>251</sup> has shown that with purified hormones effect can be produced in animals by oral administration. More recently a second estrogenic substance<sup>252</sup> "theolol" (a triatomic alcohol) has been isolated from the urine of pregnant women which is several times more active on immature female rats than theelin. Wehefritz<sup>253</sup> finds that the female sex hormone of one species is capable of producing iso-sexual changes in an animal of another species, and that the female sex hormones are biochemically identical. Engel<sup>254</sup> produced a substance in male dogs, with physiologic functions similar to the female sex hormone, by exposure of the skin surface of these animals to radium radiation. Roentgen radiation does not affect the estrus hormone but ultra-violet light renders it inactive.<sup>255</sup> It has also been shown that the female sex hormone when administered to hyacinth plants causes an acceleration of blooming.<sup>256</sup> Birch<sup>257</sup> reports that patients with hemophilia are benefited by ovarian therapy and that urine of patients with severe hemophilia is deficient in the female sex hormone. The female sex hormone has also been reported to inhibit conception in animals.<sup>258, 259</sup>

The term "progestin" was applied by Allen and Corner<sup>260</sup> to the hormone of the corpus luteum which maintains the uterus in a normal state of pregnancy in castrated rabbits. In experimental work progestin causes proliferation of the endometrium for the nourishment and implantation of ova, growth of the decidua, maintenance of pregnancy and inhibition of ovulation. In addition to these functions Smith and Smith<sup>261, 262</sup> have shown that progestin through stimulation of the suprarenal glands has a metabolic and vasomotor function. Mammary activity after gestational hypertrophy has been generally accepted as due to the corpus luteum. In Corner's<sup>260</sup> observation highly potent preparations of progestin, administered to nonpregnant animals, have failed to influence the mammary glands. It is suggested by Steinach and Kuhn<sup>263</sup> that lutein tissue produces male sex characters. (We concur with Hartman's view that the recent studies on the corpus luteum problem leave one with a diminished respect for biologic theory.)

Fellner<sup>264</sup> reviews his sixteen years' experience with the female sex hormone, which he designates as feminin. The results recorded are favorable in certain groups of cases but in most instances it has failed to give the expected clinical cures. Goldstine and Fogelson<sup>265</sup> have employed an aqueous estrus-producing hormone extracted from the placenta in 30 cases of irregular uterine hemorrhage or the so-called idiopathic climacteric bleeding and report that they were able to control the "irregular uterine bleeding" in about 25 of the 33 cases treated.

We will not attempt to discuss the recent advances in knowledge of the physiology and pathology of the anterior hypophysis in relation to the female genital organs, since this subject was recently presented in this Journal by Fluhmann<sup>266</sup> in a Collective Review of more than 170 publications.

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## Selected Abstracts

### Pregnancy and Disease

Wells, A. S.: Syphilis and Pregnancy. J. M. A. South Africa 3: 333, 1929.

In studying a series of 1000 blood examinations made in pregnant women, the author found that 28.2 per cent showed lues by the Wassermann test. In 399 tests of the placental blood 20.5 per cent were positive. He points out that this percentage is 4 to 5 times greater than that found in Europe, if compared with Gammeltoft's 5.5 per cent. He calls attention to the differences of syphilis in male and female, laying stress particularly on the latency of the disease in the female during pregnancy. He advocates Gammeltoft's provisions for eradication of syphilis as applied at present in Denmark.

FRANK SPIELMAN.



**Audebert and Aversing: The Bordet-Wassermann Test On the Milk.** *Bull. de la Soc. d'obst. et de gynéc.* 5: 420, 1931.

According to Audebert and Aversing there are two objections to performing a Wassermann reaction on mother's milk. First, there are bacteria which cannot be eliminated and which lead to errors because they develop an acidity or an alkalinity which may result in false reactions. Secondly, the readings are made very difficult and sometimes impossible by an opalescence due to gray substances. The latter cannot be removed even by centrifuging. Because of these objections the authors compared a series of Wassermann tests on the milk and on the blood of the same patients. Among 135 specimens of milk, readings could not be made in 32. In 98 cases a negative milk reaction agreed with a negative blood reaction, 1 strongly positive milk test agreed with a strongly positive blood test, 3 negative milk tests were associated with positive blood tests, and 1 positive milk test was associated with a negative blood test.

These results indicate that milk cannot replace blood for the determination of the Wassermann test.

J. P. GREENHILL.

**Abruzzese: The Passage of Bismuth from Mother to Fetus and to the Lactating Young.** *Riv. ital. ginec.* 10: No. 4, 1929.

The author made chemical, histochemical and radium researches on women and on female rabbits, examining placenta, membranes, maternal and fetal tissues, urine of fetuses at birth and during the lactating period.

He finds that in woman the bismuth is found in the placenta, but not in the fetal tissues. In the placenta, however, it is not in such quantity as to be demonstrable histologically, though it is found in greater concentration by injecting soluble rather than insoluble salts. In the urine of the fetus at birth there is no bismuth, but it appears during lactation. In the maternal urine, bismuth is found both before and during parturition. Only treatment with intramuscular injections was followed in woman.

In the female rabbits the same results were obtained with intramuscular and intravenous injections. The bismuth was found both in the placenta and in the fetal viscera both when solutions and colloidal suspensions were utilized.

SYDNEY S. SCHOCHET.

JULIUS E. LACKNER.

**Gardiner-Hill, H.: Pregnancy Complicating Simple Goitre and Graves Disease.** *Lancet* 1: 120, 1929.

Thyroid disease complicating pregnancy has been classified as: simple goiter of adolescence; simple goiter developing in adult life; primary Graves disease and secondary Graves disease. The total number of cases studied were 115, or 12, 14, 71 and 18 respectively.

In both types of simple goiter the thyroid gland hypertrophied during each pregnancy with the tendency to, or the development of a hyperthyroidism in later years. A history of sterility was found in some in whom the simple goiter had developed in adult life. In a few of both groups of simple goiter repeated abortions had occurred. In these the administration of thyroid extract seemed to prevent such terminations in later pregnancies.

The course of pregnancy was little affected when the primary Graves disease developed during the gestation. Slightly over one-half of the cases had one pregnancy after the development of this disease, but few had more. Spontaneous terminations were most likely to occur during the first four months, but after this

time full-term deliveries could be expected. The probabilities are that abortions depended more upon the severity rather than the duration of the disease.

Exacerbations of symptoms were more frequent in abortions than after delivery of viable babies. The explanation offered is that the patient's mental reactions to these endings made a considerable difference in the symptoms. An improvement in symptoms usually occurred with the advance of the pregnancy, and was augmented by mental and physical rest and treatment.

In secondary Graves disease pregnancies usually occurred before evidence of the disease. Only about 11 per cent became pregnant after symptoms of this disease were present.

The author in recapitulating states that patients with either of the simple goiters may safely be advised to conceive, providing that some form of thyroid extract be given during and after the gestation.

In primary Graves disease with favorable circumstances, adequate treatment, only little intoxication and in the absence of cardiac and other complications, a prospect of a pregnancy may be entertained. Should conception occur one cannot overestimate the importance to take every precaution to insure a full-term pregnancy.

In secondary Graves disease the prognosis appears to be even less satisfactory.

H. C. HESSELTINE.

**Ronsisvalle: Congenital Goiter in a Fetus Born from a Mother with a Goiter.**

Arch. ostet. e ginec. 17: 319, 1930.

The author describes a case of true hereditary congenital goiter. The fetal goiter was amply demonstrated by histologic slides. However, examination of the goiters of mother and fetus revealed differences: The goiter of the mother presented glandular acini of various form and size, filled with colloid. In certain places the connective tissue was scarce, in others abundant, while still in other places there was marked hyalinization of the fibrous tissue. The goiter in the fetus showed a pallid reticulated tissue with glandular formations and large capillary vessels. The glands had a cuboidal epithelium of various form with no signs of secretion.

This difference is thus explained by the author: Since the thyroid is an important regulatory organ of metabolism, diminished function of the maternal gland will affect the thyroid anlage in the fetus. This might be interpreted as the hereditary factor determining the development of all the varieties of fetal goiter, depending upon greater or lesser sensibility of the cellular elements to formative stimuli.

SYDNEY S. SCHOCHET.

JULIUS E. LACKNER.

**Gudernatsch, F.: The Administration of Thyroid Before and During Pregnancy and Its Effect on the Offspring. Monatschr. f. Geburtsh. u. Gynäk. 88: 161, 1931.**

The results of experiments with thyroid feeding which were begun in 1914 are reported by Gudernatsch. He found that when the dose of thyroid which was administered to animals was too large, symptoms of hyperthyroidism appeared such as loss of weight, diarrhea, muscular weakness, and finally cachexia and death resulted. When the dose was so regulated that the animals continued in good health they remained sterile. Conception did not occur until many weeks after thyroid administration was discontinued. In the patients where impregnation took place, one of three things occurred namely, abortion, death of the offspring shortly after birth, or in later pregnancies the young showed a tendency to retardation in growth in spite of the fact that they did not appear weak.

J. P. GREENHILL.

**Nevinny and Schretter:** Diabetes and Pregnancy. *Arch. Gynäk.* 140: 395, 1930.

The authors describe their studies on two mildly diabetic women throughout pregnancy and the puerperium. In both instances there was a marked postpartum increase in the severity of the diabetes. Both babies were unusually large and stout, being 5730 and 4750 gm. in weight and 61 and 58 cm. in length. One baby died on the twenty-eighth day, the autopsy showing a pleurisy, a bronchopneumonia and congenital heart disease. The second baby died on the thirty-second day of congenital heart disease. The blood sugar of one child was 52 mg. per 100 c.c. of blood shortly after birth and then rose to 172 mg. where it remained until death. The maternal blood sugar in the diabetic parturient rises above the average during delivery as it does in the normal nondiabetic but does not drop promptly after delivery. On the contrary it continues to rise up to 50 per cent for eight to twelve hours.

There is a difference of 28 per cent in the blood sugar of the umbilical artery blood and the umbilical vein blood. The retroplacental blood shows the same amount of sugar as does the umbilical vein blood. Blood from the maternal basilic vein shows a higher sugar content than does the fetal or retroplacental blood. The sugar content of the liquor amnii is almost as great as that of the maternal blood.

RALPH A. REIS.

**Haupt, W.:** The Question of Interrupting Pregnancy Because of Status Epilepticus. *Monatschr. f. Geburtsh. u. Gynäk.* 83: 16, 1929.

In half of all epileptic patients who become pregnant, the epileptic condition becomes aggravated. Only one-quarter show an improvement but this does not extend beyond the puerperium. The first appearance of epilepsy during pregnancy is rare. In 10 of the reported 19 cases of epilepsy associated with pregnancy death resulted. Most of the patients were treated conservatively. The author reports a case of his own where in the fourth month, the epileptic symptoms were suppressed by lumbar puncture and injection of air, followed by interruption of pregnancy and sterilization. The patient recovered.

J. P. GREENHILL.

**Glas, Rudolph:** A Case of Taboparalysis, Malarial Treatment, Subsequent Labor. *Zentralbl. f. Gynäk.* 53: 3458, 1929.

A forty-three-year-old primipara had been treated with malaria eight years previously for a progressive paralysis, although there had been no history of lues. She was seen in the psychiatric clinic during the present pregnancy because of suicidal tendencies, and blood and spinal fluid Wassermanns were found to be positive. Premature delivery occurred about the seventh calendar month, resulting in a 1320 gm. twin which died in twenty-nine hours and a 1500 gm. stillborn. The patient died subsequently from what seemed to be an intrapartum infection. A feature of the delivery was absence of pains except when the head passed the perineum. Strassmann reported a similar case, taboparalysis, resulting in delivery of a healthy child, and Weissmann has observed the birth of two healthy children from a mother who had received malarial treatment for progressive paralysis.

Despite the present case, the author believes the prognosis in subsequent pregnancies after malarial treatment to be good.

WILLIAM F. MENGERT.

**Bernardi:** Postencephalic Parkinsonism and Pregnancy. *Arch. obstet. e ginec.* 17: 273, 1930.

From the systematic study of a pregnant woman with a classical post-encephalic parkinsonion syndrome, observed for six months, the writer concludes: The pregnancy exaggerated the manifestation of the disease. No modifications were

observed in the reactions and morphologic components of the blood. Hyperglycemia which seems a characteristic finding in postencephalic parkinsonism failed to appear throughout the pregnancy. Scopolamine hydrobromide which had a marvelous therapeutic effect gave rise to a slight hyperglycemia. Changes in the electrolytic equilibrium of the blood lead to a slight hypopotassemia and hypercalcemia.

The patient was dismissed, cured by means of the medical therapy, and the child was free from any abnormality.

SYDNEY S. SCHOCHET.

JULIUS E. LACKNER.

Bacialli: The Treatment of Fibroma in Pregnancy. *Osp. maggiore di Novara* 8: 691, 1930.

The author discusses the technic of myomectomy on a pregnant uterus which does not greatly differ from that employed in the absence of pregnancy. To do this operation can be decided only after the abdomen has been opened. In some cases one is forced to perform hysterectomy.

The author favors this type of operative intervention, both for its immediate and remote effects. There is the possibility of removing a cause for abortion; there remains the chance for a new pregnancy. The sexual life of the patient will continue normally.

SYDNEY S. SCHOCHET.

JULIUS E. LACKNER.

Phaneuf, L. E.: Myomectomy During Pregnancy. *New England J. Med.* 202: 565, 1930.

Myomectomy during pregnancy is usually done for pain, aseptic necrosis, compression of bladder or rectum, torsion of pedicle, incarceration in front of the presenting part, and for incarceration of a retroflexed myomatous uterus. In this case the operation was required in the fourth month by severe and persistent pain. The amniotic sac was exposed for an area of about 5 cm. in diameter, but pregnancy went to full term. Disproportion between pelvis and head finally required delivery by cesarean section.

HUGO EHRENFEST.

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## Item

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### AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY

#### GENERAL STATEMENT

The organization of this Board is the culmination of a determined effort on the part of the American Association of Obstetricians, Gynecologists, and Abdominal Surgeons, the American Gynecological Society, and the Section on Obstetrics, Gynecology, and Abdominal Surgery of the American Medical Association, to improve the standards of practice of obstetrics and gynecology in the United States and Canada, and to formulate a means of general discrimination between the truly qualified obstetrician and gynecologist, as contrasted with the self-styled "specialist."

The Board does not, by its Certificate, confer any special degree or license to practice obstetrics and gynecology, nor does it desire to inter-

fere with the professional activities of any regularly licensed physician. It does propose, however, to standardize qualifications for specialists in these branches, and to furnish certificates to those who comply with these requirements.

These are, in general terms, that one must have had a certain minimum amount of special training, must satisfactorily demonstrate his ability in the specialty, and must be limiting his work to the specialty according to a broad definition of this latter outlined in the booklet issued by the Board. An applicant's record and credentials are carefully scrutinized, a series of case records submitted by him are examined in detail, (except where men have specialized for more than ten years and have official hospital appointments during this time), and he is obliged to meet in person with the Board to undergo an oral and clinical bedside examination to demonstrate his ability.

These requirements are rigid and arduous but any well qualified obstetrician and gynecologist should have no difficulty in obtaining the certificate. Rigid requirements constantly maintained will make the certificate more and more valuable to its possessor. The present high standards of the Board and the desirability of its Certificate are attested by the distinguished list of Diplomates and there can be no argument for lower standards.

For further information regarding requirements, dates and places of coming examinations, and application blanks address the Secretary, Dr. Paul Titus, 1015 Highland Building, Pittsburgh, Pennsylvania.

#### ANNOUNCEMENT OF EXAMINATIONS

The next written examination of the American Board of Obstetrics and Gynecology will be held on Saturday, October 22, at 2 P.M., in 19 different cities of the United States and Canada (see announcements). In order to reduce traveling expenses for candidates special arrangement may be made through the Secretary for taking the written examination at any city other than those regularly specified where there is a Diplomat who can be empowered to conduct the examination. This arrangement does not apply to the general, clinical examination to be announced later. For further information address, Dr. Paul Titus, Secretary, 1015 Highland Building, Pittsburgh, Pennsylvania.

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#### Errata

In the May number of the Journal, page 761, there appeared a case report by Dr. Sol. Litt. Through error in transmitting this report the names of Dr. Julius Lackner and Dr. Lester E. Frankenthal, Jr., were omitted as co-authors.

The title as corrected should read: Drs. Julius Lackner, Lester E. Frankenthal, Jr., and Sol. Litt reported a case of Double Uterus.

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## Original Communications

### ON CERTAIN ENDOCRINE FACTORS IN MENSTRUATION AND MENSTRUAL DISORDERS, WITH SPECIAL REFERENCE TO THE PROBLEMS OF MENSTRUAL BLEEDING AND MENSTRUAL PAIN\*

EMIL NOVAK, M.D., BALTIMORE, MD.

*(From the Gynecological Department of Johns Hopkins Medical School)*

THE endocrines, or chemical messengers, represent a stage-coach era in the intercommunications of the body, and they still play the chief rôle in the mechanism of functions where speed is not such an essential as certainty and automaticity. In the more highly volitional functions, such as those of skeletal muscle contractility, the more cumbersome stage-coach method of carrying impulses has been superseded by the telegraphic system of the nerve apparatus. The nerves of the body, in this sense, may be looked upon as a sublimation of the more primitive endocrine system. When one touches a hot stove, disastrous results would follow were the afferent sensory impulse to the brain or the efferent motor-impulse to the muscles of the arm carried by chemical messengers through the blood stream. Here the messages must be flashed by some more rapid medium, and hence the evolution of the medullated nervous system.

With the more primitive vegetative functions of the body, of which reproduction is one, the dominating rôle is still played by the endocrine apparatus, so that the story of reproductive physiology is largely a story of its endocrine mechanism. It is an intricate but fascinating one, extending from the egg to the grave. Many of the chapters are still lacking, but enough have been brought together to impress us with the marvelous purposefulness of the endocrine influence which is responsible

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NOTE: The Editor accepts no responsibility for the views and statements of authors as published in their "Original Communications."

for the conception, nidation, prenatal and postnatal life of every human being, which is responsible for many of his individual physical and perhaps mental attributes, and which in turn, confers on him the privilege of immortalizing these by propagating his own species. Let us sketch briefly some of the endocrine influences which mold the destinies of the human egg, through the elaborate perfection of a cyclical mechanism designed to convey it in a fertilizable condition to its tryst with the spermatozoon, to shelter and nourish it until its maturity, and then to deliver it safely to a waiting obstetrician. All the resources of the mother's body are made available for this supreme function of propagation of the race, so deeply rooted that organs far distant, like the hypophysis at the base of the brain, contribute important parts in the drama enacted on the pelvic stage.

Even in the fetal life of the future mothers of our race the endocrines play a part which must, according to an increasingly prevalent view among embryologists, be important, though as yet mysterious. As applied to the reproductive apparatus, it seems natural to believe that the early differentiating processes in the genital canal must be under the influence of an endocrine mechanism, as yet unknown. The germinal epithelium of the ovary, the tubal mucosa, the endometrium, the endocervix, and the vaginal mucosa, all are products of the differentiation of the primitive coelomic epithelium. We can only speculate as to the forces behind this differentiation, but the fact that corresponding changes in adult tissues are of known endocrine origin makes one feel that similar forces play a part in these fetal processes.

We are equally in the dark with regard to the developmental changes in the sex gland area, with the final product of an apparently complete female gonad, so different in structure from the male at this stage, and yet so indistinguishable in an early phase. Once differentiated the ovary remains latent until the vivifying spark of puberty is touched off, and it is here that the story begins to take on a little more form and substance. What force constitutes the puberty spark we can not be sure, but we do know that, in animals, the implantation of anterior hypophyseal tissue will bring on puberty long before the normal time, so that it seems probable that this gland must in some way start the reproductive machinery at puberty. The immediate effect in the ovary of the girl, as in the experimental animal, is the maturation of graafian follicles. That follicle growth, to at least a limited degree, is seen before puberty, suggests that there may be at least some hypophyseal activity in young individuals.

The puberty impulse, then, results in maturation changes in a large number of follicles, but of these only one every moon is destined for complete maturity and ovulation. What factors determine this selection of a single follicle from among many hundreds of similar structure we do not know. Furthermore, it is quite certain that ovulation does not

always occur, as it probably does in later life, as soon as follicle maturity is attained. The mere distention of the follicle with liquor folliculi is not enough to ensure ovulation, for much greater distention is seen in many atretic follicles. Some other ovulation factor is required, and here again the hypophysis seems to be concerned, as shown in the experimental work of Friedman<sup>1</sup> and others, and as utilized in the now well-known Friedman test of pregnancy.

There are some who believe that the hormone of the mature follicle exerts a reciprocal effect upon the hypophysis, bringing about a discharge of the ovulation principle, presumably the luteinizing hormone of this gland. The evidence for this is not at all complete, especially as other investigators, notably Leonard, Meyer, and Hisaw,<sup>2</sup> have found that injections of theelin bring about an inhibition of pituitary function, with consequent atrophy and finally sclerosis of the ovaries.

The logical hypothesis would be that the theelin perhaps inhibits further motivation of the follicle-maturing hormone, for this would coincide with our concept of the sequential action of the two pituitary principles. The evidence for this, however, is not in hand. The normally fine dovetailing of these hormones is readily disturbed. For example, as already stated, ovulation may not occur even if the follicle is fully mature. The persistence of such unruptured follicles, giving off large amounts of theelin, can produce an exaggerated proliferation or hyperestrous picture in the endometrium, a condition which we recognize in the laboratory as hyperplasia of the endometrium, and which clinically is so often associated with functional bleeding.

As we shall see, however, the bleeding is not due to the mere excess of folliculin, but to some other factor. Indeed, amenorrhea may be associated with excessive production of theelin, and with hyperplasia of the endometrium. The work of Frank<sup>3</sup> and his collaborators indicates that the overproduction of theelin has little significance unless one takes account also of the rate of its excretion through the kidneys. The point which I wish to stress at present is that a rather fine adjustment of hormone action is essential for the first menstruation, and, for that matter, of succeeding ones as well. If the follicle maturing apparatus of the hypophysis and the ovary begin to operate before the luteinizing mechanism is unlimbered, the girl will exhibit periodic hemorrhage, i. e., menstruation, without ovulation. I believe that this phenomenon, which formerly would have been considered paradoxical in the human being, must occur in many girls at puberty and also in many women at the menopause, where again the usual "one-two" action of the follicle-ripening and luteinizing hormones, as demonstrated by Fevold, Hisaw, and Leonard<sup>4</sup> in a recent paper, is readily upset.

With regard to the hormonal mechanism of the menstrual cycle itself, little need be said in this paper, especially as I have discussed this at length in several recent publications.<sup>5</sup> It is now quite universally ac-



cepted that the two ovarian hormones, folliculin and progestin, are responsible, respectively, for the proliferative and the secretory phases of endometrial development, and that their formation and activation is contingent upon the two sex hormones of the anterior hypophysis, i. e. (1) the follicle-ripening hormone, or Prolan A, or rho 1, as it is variously called; and (2) the luteinizing hormone, or Prolan B, or rho 2. That there are really two such hypophyseal principles is accepted by all except a few investigators, the latter believing that the different effects are merely phases or degrees in the activity of a single sex hormone.

The theory of "the primacy of the ovum" as a regulator of menstrual periodicity, and the hitherto universally accepted belief that menstruation is dependent upon ovulation have likewise, I believe, been discredited by recent investigators, as I have shown in a previous paper.<sup>5</sup> The former of these was in its very nature always speculative, and its abandonment so far has meant simply a shift from one theory to another, equally speculative. But the feeling that ovulation is a necessary precursor of menstruation was one which had entrenched itself in the minds of those interested in gynecologic histology, for certainly in the human being ovulation does characteristically precede menstruation. The most important evidence that ovulation is not indispensable to menstruation has been furnished by Hartman,<sup>6</sup> Allen,<sup>7</sup> and Corner,<sup>8</sup> all of whom find that in monkeys, under certain conditions, periodic bleeding continues even when no follicles or corpora lutea are to be found in the ovaries. To all intents and purposes this bleeding represents menstruation, in a clinical sense, at least.

On the other hand, it does not, strictly speaking, correspond to menstruation as it occurs in the human female. To this extent, I believe that Meyer is right in insisting that a distinction be drawn between human menstruation, with its preceding ovulation, corpus luteum formation, and pregravid endometrium, and the type of periodic hemorrhage described by Hartman, Allen and Corner. For that matter, it seems to me, that, surveying the entire animal scale, at least three types of periodic genital hemorrhage are distinguishable. First there is the type seen in monkeys during the nonbleeding, nonovulating summer season, in which the bleeding is the result of some extraovarian factor, probably emanating from the anterior hypophysis, according to the work of Hartman, Firor, and Geiling.<sup>9</sup> This type has not yet been demonstrated in the human being, though it may perhaps occur.

The second variety, seen at times in the human body, is associated with excessive amounts of follicle hormone emanating from persistence of mature follicles. In these cases it is not at all certain that the folliculin in itself is the cause of the bleeding. Indeed, the evidence, from our human material at least, is against the view. These are the cases which we group as functional hemorrhage, with hyperplasia of the endometrium. But the endometrial condition, which undoubtedly, in

the light of recent investigations, is due to the excessive follicle hormone stimulation, with a pituitary causation in the background, is a persistent stationary one, and the bleeding in most cases is distinctly periodic. In other words, there must be a periodic addition or subtraction of some unknown factor to explain the bleeding. In the nonbleeding phase, the endometrium is still hyperplastic, and indeed, one may find hyperplasia in women who have been amenorrhoeic for months. The periodic factor responsible for the bleeding in these cases is probably the same as the one responsible for the first group, although the ovarian and endometrial findings are very different.

The prototype of this variety of bleeding, in the human cycle, is the interval or intermenstrual type of bleeding occasionally observed in women, often with intermenstrual pain. It corresponds to the maximum of follicle development, and is therefore to be compared with the estrous type of bleeding in some of the lower animals. In its very common pathologic form, abnormal functional hemorrhage, we have to do with an excess of follicle hormone, and a hyperestrous rather than an estrous endometrium. To put it another way, the characteristically periodic bleeding of hyperplasia is not really a menorrhagia but an exaggerated estrous or intermenstrual bleeding, for menstruation in the stricter sense above outlined is completely absent.

Schröder,<sup>10</sup> Tietze<sup>11</sup> and others explain the bleeding in these cases as due to small localized areas of necrosis in the endometrial surface, although they of course accept that the underlying cause is the endocrine imbalance indicated above. We have found such localized necroses much less frequently than the above mentioned authors, and it seems difficult to believe that such small defects could be the cause of such massive hemorrhage as one may see in cases of the functional type. In normal menstruation, when the whole endometrial surface is commonly lost, the hemorrhage is much less. I believe that some other factor must be at play in our functional cases, and that this produces an increased permeability of the blood vessels of the endometrium, so that profuse pouring out of blood elements, by diapedesis, can occur with little or no loss of surface tissue. It is even conceivable that the necrobiotic areas stressed by Schröder are due to the hemorrhage, rather than vice versa.

Finally, as regards the bleeding of normal menstruation in women, the conditions are again quite different. Here we have an endometrium built up under the influence and protection of a maturing corpus luteum, and the purpose of this is concededly in the nature of a preparation for the reception of a fertilized ovum. If this purpose is frustrated, i. e., if fertilization does not occur, the corpus luteum retrogresses and the endometrium is cast off. The bleeding associated with this casting off is what we call menstruation. That this is due to the withdrawal of the corpus luteum hormone is strongly suggested by the fact that excision of a corpus luteum before the expected menstrual period precipitates the

latter, as has been observed by many gynecologists. On the other hand, excision of a mature follicle will likewise be followed by bleeding. Furthermore, since the human corpus luteum also contains folliculin, it may well be the withdrawal of the latter which is responsible for the bleeding after corpus luteum excision.

I mention these facts because Hartman<sup>12</sup> has suggested that the bleeding of menstruation may be due to a positive rather than to a negative factor; that is, that it is due to something added to the endometrium rather than something withdrawn. His valuable observations on other types of periodic bleeding, in which he has clearly shown that such a positive factor must exist, would naturally lead him to similar views regarding the bleeding of the ovulatory type of cycle seen in the human being. But the conditions here are very different, as I have pointed out, and I believe that the evidence still indicates that here we have a genuinely catabolic process, a sort of house-cleaning, with degeneration of the corpus luteum, decidualation of the menstrual endometrium, and a bleeding comparable to that of the actual decidualation of pregnancy, in short, essentially, an "abortion of an unfertilized egg."

In the event, however, of the egg being fertilized, the further uterine changes are anabolic rather than catabolic. The persistence in function of the corpus luteum of pregnancy has an obvious purposefulness, for it preserves the integrity of the endometrial bed which has been prepared for the egg. Furthermore, the corpus luteum hormone inhibits uterine contractions in both the pregravid and early gravid phases. Folliculin, as has been shown by Reynolds,<sup>13</sup> increases the responsiveness of the uterine and tubal muscle. With fertilization such muscular contractility would presumably interfere with nidation, and its inhibition by the corpus luteum hormone serves a definite purpose during this period, before the embryo has become firmly anchored in the uterus. In addition the corpus luteum inhibits further ovulation, although at a later phase abundant folliculin is found in the placenta and is probably produced by it.

There is one other physiologic aspect of cyclical activity to which comparatively little attention has been directed until very recent years. I have already alluded to it, but inasmuch as it may have a bearing upon some of our clinical problems, it may be reemphasized. I have reference to the variations in the rhythmic contractions of the uterus observed at different phases of the cycle. A number of studies on this problem have been made within recent years, and the results have not been uniform. Perhaps the most thorough and careful investigations have been made by Knaus<sup>14</sup> in Austria, and Reynolds<sup>13</sup> in this country. The method employed by Knaus in his experimental investigation was to test the response of the uterine muscle to posterior pituitary extracts after previous treatment with various dosages of the two ovarian hormones, folliculin and progesterin. He found that the folliculin-treated uterus was

increasingly responsive to pituitrin with increasing dosage of folliculin. On the other hand, progestin produces refractoriness of the uterine musculature in this respect, with failure of response to the pituitrin stimulation.

The ingenious technic employed by Reynolds is quite different and apparently much more trustworthy, for it gives an opportunity of studying the uterine contractions of the experimental animal in the unanesthetized state. The upper portion of the rabbit's vagina is cut across, the lower end turned in and buried, while the upper end is brought out through the abdominal wall, to which it is sutured. Through the fistula thus created ready access is given to the animal's two uteri. Through the introduction of a small balloon into the uterus, the effects of various stimuli upon the uterine contractions can be readily studied and recorded by an air-water manometer with kymographic attachment.

By this method Reynolds has shown that the estrous phase in the nonpregnant rabbit is associated with marked uterine activity, while anestrus, on the other hand, is characterized by only feeble activity, or none at all. Furthermore, castration produces a progressive lessening and irregularity of contractions, with eventually complete quiescence. By replacement therapy with theelin in castrated animals, the uterine motility can be restored to normal, thus demonstrating that theelin is the factor concerned with this property.

On the other hand, by the study of animals in the phase of pseudo-pregnancy, associated with corpus luteum activity, he has shown that the corpus luteum secretion brings about a quiescence of the uterine musculature. Finally, he has demonstrated, by the same uterine fistula technic, that the injection of the urine of pregnant women, like that of progestin, inhibits uterine motility, while the urine of nonpregnant women produces no effect whatever. For the details of these experiments, here merely sketched, I would refer the reader to Reynolds' original papers.

What bearing do such physiologic demonstrations as this have upon our concept of menstruation or upon the question of menstrual disorders? One must always hesitate in applying to one species conclusions based on the study of another, but the fundamental fact that theelin is a stimulant and progestin (or the luteinizing hormone principles of the urine of pregnant women) an inhibitor of uterine motility is in strict consonance with our existing knowledge of the human reproductive cycle, and with a few studies which have been made upon the human subject. Translated to the human problem these observations indicate that the rhythmic contractility of the tubal and uterine musculature becomes progressively more marked as the follicle grows, with its maximum just before ovulation. With the discharge of the ovum, the contractions are inhibited, so that during the progestin phase the tubal and uterine muscle is relatively quiescent. This mechanism makes possible a slow

passage of the ovum through the tube, and protects it from premature discharge, before ovulation, from the uterine cavity.

As applied to the menstrual cycle, the rhythmic contractions become increasingly marked up to about the middle of the intermenstrual cycle, and the genital muscle is relatively quiescent beyond this, especially in the progravid or premenstrual phase. Clinically one occasionally encounters patients with normal pelvic organs who suffer from intermenstrual pain or bleeding, or both, at a time in the menstrual cycle which corresponds with maximum follicle activity, i. e., at a phase which corresponds to estrus in the lower animals. The bleeding in these cases, usually slight in amount, is apparently the analogue of the estrous bleeding seen in many animals, and, as already discussed, is due to theelin activity. The pain, well recognized clinically as "intermenstrual pain" (*mittelschmerz*) is logically explained, it seems to me, by the fact that the rhythmic contractions of the uterus reach their maximum at this phase, and, under certain conditions, may be perceived by the patient as a genuine pain.

A far more important bearing of this general doctrine, it seems to me, is in the possible explanation of primary dysmenorrhea, one of the bugbears of gynecology. I need not, before this audience, stress the great prevalence of this disorder, the suffering and invalidism which it entails, the inadequacy of all the explanations which have been offered as to its mechanism, and the unsatisfactoriness of its treatment. That many factors may enter into its production admits of no reasonable doubt. In some cases it is undoubtedly psychogenic in origin, in others it is secondary to constitutional deficiencies of one sort or another, in a small group it may be of obstructive type.

No one, so far as I know, has considered the possible etiologic relationship of a disorder in the cyclic rhythmicity of uterine contractions. And yet, it seems to me, this is the logical concept. For example, whatever the underlying disturbance may be, the pain in primary dysmenorrhea is characteristically of a spasmodic, colicky nature, suggesting as the immediate cause, a painful, exaggerated contractility of the uterine musculature. Secondly, in the typical case the pain begins a day or two before the onset of the flow, at just the time that the corpus luteum begins to degenerate, for retrogression is not ordinarily followed by the bleeding of menstruation until the lapse of a considerable interval. For example, if a corpus luteum is excised several days before menstruation is due, menstruation is precipitated, but usually not until from twenty-four to forty-eight hours.

The removal of the corpus luteum influence brings about a rapid return of uterine contractions, and, indeed, Knaus has found by direct studies on menstruating women, that this is the period of maximum contractility. Here again, and especially in women whose threshold of pain is lowered because of psychic, constitutional, or developmental factors,

we have a logical explanation of this type of dysmenorrhea. In recent years there has been a tendency to explain these cases as due to a hypoplasia or underdevelopment of the uterus, just as formerly they had been explained on the theory of mechanical obstruction in the cervical canal, as a result usually of antelexion. The inadequacy of both of these theories must be patent to everyone who has studied any large number of these cases. For example, as regards the factor of hypoplasia, a disconcerting fact has always been that many of these patients have no pain for perhaps a good many years after puberty, but later begin to suffer intensely.

I have merely indicated here the general principle involved in the explanation which I have suggested. There are many other aspects which might be discussed, the possible rôle of an imbalance between follicle and corpus luteum secretions, the probability that the underlying rôle is often played by the hypophysis, the part played by pregnancy and parturition in the relief of this type of disorder, and so on. Some of these, at any rate, will be discussed in a forthcoming paper by Reynolds and myself, based on the former's physiologic studies of uterine motility.

The considerations above set forth suggest that the treatment of primary dysmenorrhea must take into account not only psychogenic, constitutional, developmental and local anatomic factors, but that the relief of the pain itself may perhaps be just as effectively, and more intelligently, accomplished by certain hormonal agents than by the mere administration of anodyne drugs. So far as I know the only substance which is available for this purpose in the human being, and which has been experimentally demonstrated (Reynolds) to have an inhibiting effect upon uterine contractility, is the so-called luteinizing substance prepared from the urine of pregnant women. This I have used as a *part* of the treatment of a number of cases of primary dysmenorrhea, although it is of course too soon to discuss results. This is particularly true since we are dealing with a subjective disorder in the etiology of which a number of factors may be involved.

In this paper I have tried to avoid a discussion of what has come to be the generally accepted view as to the humoral mechanism of menstruation itself, and have limited myself to the discussion of one or two of the less generally recognized factors involved in the process, more particularly in their bearing upon the problems of menstrual bleeding and menstrual pain. Each year the experimental workers in this field, comprising many of our best anatomists and physiologists, are giving us new facts to apply in the interpretation and management of our clinical problems. This imposes on us the obligation to use this ammunition honestly and intelligently.

No gynecologist nowadays can afford not to keep in close touch with the rapid progress being made in the experimental investigation of the

reproductive cycle, for an increasing number of our clinical problems are seen to be of functional rather than organic causation. The day of endocrinologic joy-riding is happily gone by, for we have advanced to an era in which the cool-headed scientist is at the wheel, with his foot constantly on the brake rather than the accelerator. I, for one, am willing to ride with him rather than behind the irresponsible commercial or pseudoscientific chauffeurs who still clamor so noisily, and often so successfully, for gullible passengers.

#### SUMMARY

Most of what we know concerning the physiology of menstruation pertains to its endocrinology, for the fundamental rôle in the mechanism of this process, like that of most other vegetative functions, is still played by the endocrine system rather than by the more highly developed nervous apparatus which is so important in such volitional processes as skeletal muscle contractility.

The endocrine factors are probably important even in the fetal and prepubertal epochs, but at puberty their function becomes much more important and more conspicuous. Much has already been learned concerning the respective rôles played by the two ovarian secretions, folliculin and progesterin, in the reproductive cycle, and much is being learned as to the relation, apparently subordinate, of these two hormones to the two corresponding sex hormones of the anterior hypophysis.

Such menstrual abnormalities as excessive functional bleeding can not be studied in mere terms of endometrial histology or even of quantitative blood hormone content. A broader viewpoint, based on considerations of comparative physiology, helps much in the interpretation of such problems. For example, periodic hemorrhage from the genital canal may be of various types, each with an entirely different mechanism, as discussed in the paper. The most common variety, encountered clinically as functional bleeding with hyperplasia of the endometrium, is apparently due to a persistence and excess of the follicle secretion, with deficiency or excess of the corpus luteum hormone, progesterin. There can be little doubt, however, that this immediate ovarian disturbance is in turn due to an imbalance of the governing sex hormones of the pituitary.

Recent work on the problem of uterine motility indicates that this is subject to a definite cyclical influence, that folliculin is in general a stimulator and progesterin an inhibitor of the rhythmic uterine contractions. I have therefore advanced the view that the pain of primary dysmenorrhea is explainable, in part at least, on the basis of these facts. This pain is characteristically of a colicky type, suggesting spasmodic muscle contraction, and it begins characteristically a day or two before the onset of menstrual bleeding, i. e., just at the time that the withdrawal of the inhibiting corpus luteum hormone takes place. While various

other factors undoubtedly play a rôle in the production of primary dysmenorrhea (psychogenic, constitutional, developmental, etc.) the immediate cause would seem to be in a heightened irritability of the uterine muscle. On this basis, a very tentative suggestion as to a plan of organotherapy is made, to be combined, of course, with measures directed toward other such factors as those mentioned above.

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26 EAST PRESTON STREET.

(For discussion, see page 447.)

## A STUDY OF THE ESTRUS-PRODUCING HORMONE IN THE CIRCULATING BLOOD OF NORMAL WOMEN

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IF THE Frank test for the determination of the concentration of the estrus-producing hormone in the circulating blood is to prove of value in differentiating types of endocrine disturbances associated with irregularity of menstruation, or in formulating more accurate prognoses in these cases, the constancy of cyclic variation of this substance in the blood of normal subjects during the menstrual cycle must be thoroughly established. Although there are various reports based on a single test or rarely on repeated tests in large groups of normal women in whom the majority of specimens of blood taken during the week preceding the menstrual period shows an increase of the hormone in the blood, we have felt that an investigation of a group, with frequent tests on the same subject, would be of value in establishing more accurately the duration of the increased concentration of hormone, and in ruling out variations (in hormone level) during the interval. Five women who experienced regular menstrual cycles volunteered for this study and tests were made semi-weekly. In one case the experiment was carried on over a period of three months, in the second case for two months and then interrupted for two



weeks because of fall in hemoglobin content and erythrocytes, and resumed in the third menstrual period. In two cases the period of study was one month, and in one case the period of study extended through two cycles.

The method of extraction of the estrus-producing hormone, which Frank calls "the female sex hormone," was described by Frank and his coworkers in 1925. In 1926, Frank and Goldberger reported the results of studies with this test on normal subjects and on patients with normal menstrual cycles. They found in most of the tests taken between the twenty-third and tenth day preceding a menstrual period, that the 40 c.c. of blood required for the test did not contain a quantity of hormone sufficient to produce the estrus reaction in a castrated white mouse. Estrus was produced in the experimental animal from 44 per cent of subjects tested from the tenth to the third day before the menstrual period, whereas Frank in his earlier studies found the reaction to be produced in 100 per cent from the third to the first day preceding the menstrual period. He subsequently found that concentration of the hormone increased in a very small proportion of cases in this period. Immediately after the onset of menses the concentration of the hormone in the circulating blood was found to drop abruptly. Frank concluded that following ovulation, which is believed to occur usually at fourteen days before the anticipated menstrual period, a latent time of approximately four days is necessary before the hormone is present in sufficient concentration to be demonstrated in the blood. During the normal sex cycles the hormone accumulates in the circulating blood until menstruation sets in.

Frank made 172 tests on 97 subjects with normal cycles. A few cases in which five or six tests were made at intervals of from four to ten days are cited. The level of hormones between the individual tests is assumed to correspond with the general level indicated by a compilation chart of all tests.

Hirsch, in 73 tests (68 done with Frank's technic), established with a composite chart a curve of hormone level closely corresponding to that found by Frank. In a few cases three or four tests were made on the same subject. Janney, modifying Frank's method of extraction of the hormone in several particulars, found in 203 satisfactory tests results decidedly at variance with those of Frank; a large proportion of reactions were negative immediately preceding menstruation.

Mazer advocated the withdrawal of 80 c.c. of blood in each test to permit duplicate tests to be made because of low sensitivity of certain animals to the action of the hormone.

In our studies the technic described by Frank was followed exactly. The specimens of blood were secured in the morning before breakfast and the preparation of the extract was started immediately. The hormone was extracted in the Section on Chemistry of The Mayo Clinic. The ether extract was allowed to dry overnight, the aqueous solution of the residue was prepared the following morning and the first injection was made shortly thereafter. The experimental animals had been carefully oophorectomized and daily vaginal smears had been taken for at least two weeks before the animals were used. The daily smears were continued throughout the course of the experiment. Cycles returned in a small proportion of mice, probably because of incomplete removal of the ovaries. Because of the very small structures involved, the surgical technic is difficult. Parkes, Fielding, and Brambell noted reappearance of estrual cycles in about 9.1 per cent of mice in which the ovaries and the proximal end of the fallopian tube had been removed. They sug-

gested that regeneration of ovarian tissue occurs, since any remnant of tissue left at operation would continue the cycles without interruption. In three of our experiments the first spontaneous cycle apparently coincided with the time of experimental injection. This was indicated by the rather atypical development of the estrus in relation to the time of administration of the hormone, and by the appearance of the second estrual cycle after an approximately normal interval.

Numerous hemoglobin determinations were made. There was no appreciable change in values in the three subjects who were given the tests for one month. In the second and third subjects who were studied over a period of three months there was a gradual decrease in the hemoglobin and in the level of erythrocytes. This factor was of sufficient significance to prevent continuing the tests longer than three months or securing specimens of blood oftener, and also precluded the use of duplicate tests as recommended by Mazer.

#### RESULTS

Seventy-one tests were made. Five mice died during the administration of the hormone and vaginal smears were not secured. Spontaneous estrual cycles obscured the results in three tests, leaving sixty-three completed and satisfactory tests. Table I indicates the results of the tests in their relation to the menstrual cycle. More than one month is included in the table to show more correctly the sequence of tests which were started at varying times during the menstrual cycle.

In the twenty-six satisfactory tests made from the tenth to the first day preceding menstruation, the results in five were positive in five different cycles in three subjects; in twenty tests the results were negative. A positive reaction was not encountered on two consecutive tests during the premenstrual period. During the days of menstruation the tests on two subjects gave positive results in three different cycles; in one case the reaction was positive both on the first and fifth day of menstruation; in a second cycle of the same subject a positive reaction was noted on the fifth day of menstruation and also on the second day following menstruation. In the interval from the last day of menstruation to the tenth day preceding, three tests on three different subjects gave positive results and nineteen tests gave negative results.

#### COMMENT

Although our study was made on a small group of subjects, we question the practical value of the Frank test. Positive reactions offer valuable data in regard to the functional activity of the ovaries, but a negative reaction, even in the ten days preceding menstruation, seems to be of little diagnostic or prognostic value. Our studies have indicated that the increased concentration of hormone is of relatively short duration, and that negative results frequently follow tests on normal subjects during the premenstrual period, whereas positive results may occur at any time

TABLE I. SUMMARY OF RESULTS\*

SUBJECT	MONTH	DAYS PRECEDING MENSES												MENSTRUAL PERIOD					POSTMENSTRUAL PERIOD										
		24	23	20	19	17	16	15	13	12	11	10	9	8	6	5	3	2	1	1	2	3	4	5	6	8	9	12	14
1		0		0		+			0				**	0		0		0	0						0				
2																0			+	***									
3	First									0						0					0								
	Second						0										0				0								
4	First										+					0					0								
	Second	+		0		0					0						+				0								
	Third			Test interrupted						0						0		***	0		0		**						
5	First															0			+										
	Second		0	0			0						0			0					0								
	Third			0			0									0					0				+		+		

\*0 denotes negative reaction; + denotes positive reaction.

\*\*An atypical reaction which proved to be a first spontaneous estrual cycle for test animal; whether test was positive also cannot be determined.

\*\*\*Mouse died from toxicity of extract before test was completed.

during the interval. We experienced difficulty in the use of the test from the apparent toxicity of the extract which caused the death of certain experimental animals before the test was completed, and from the recurrence of spontaneous estrual cycles in a small proportion of the mice. Mazer emphasized that the sensitivity of mice to the reaction varies, and he recommended duplicate tests in each instance. The amount of blood required for this, with the inconvenience to patients of repeated puncture of veins, prevents repeated studies of any particular case which we believe are necessary in view of the variable occurrence of the increased concentration of hormone in relation to the menstrual period.

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### UTERINE ALLERGY

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UTERINE symptoms due to food allergy need definite consideration.<sup>1</sup> The abundance of smooth muscle and of mucous membrane in the tubes, uterus, and vagina emphasizes the probability that allergic reactions may occur in this tract. Food allergens after their entrance into the blood should be able to produce edema of mucous membrane and smooth muscle spasm in the female genital tissues, as they do in the bronchial tract where they result in bronchial asthma,<sup>2</sup> or in the nervous system where they produce migraine or neuralgia.<sup>3</sup> Moreover in experimental allergy, uterine strips have long been utilized for the graphic demonstration of specific sensitization in the guinea pig. The occurrence of allergic disturbances in definite locations in the body depends on the well recognized tendency of localization of allergy in varying tissues in different individuals. Thus some patients have cutaneous or bronchial symptoms from food allergy while others have nasal or gastrointestinal symptoms. In women uterine allergy is not so common as the aforementioned types, but it occurs rather frequently and deserves recognition.

#### LITERATURE

Duke<sup>4</sup> in 1923 first reported painful and frequent menstruation relieved by avoiding foods to which allergy existed. In 1928,<sup>5</sup> I confirmed his opinion that food allergy could produce disturbed menstrual function, and early in 1931, I stated that I was "more convinced of the rather frequent occurrence of uterine discomfort and dysfunction due to food allergy." In the same publication, I stressed the

probability that certain menstrual symptoms in patients with migraine, urticaria, bronchial asthma, bladder allergy, hay fever, or gastrointestinal allergy might be due to food sensitizations. The fact that leucorrhea could result from food allergy in the same way that the mucous discharge in certain cases of perennial hay fever is due to such allergy was recorded<sup>1</sup> for the first time in the literature. This was originally suggested to me by my associate, O. H. Garrison. Since then Smith<sup>6</sup> has reported 12 patients with essential dysmenorrhea, leucorrhea and irregular periods who were relieved by the elimination of specific foods. The causative foods were determined by the scratch test, delayed reactions being recorded. His comment that most physicians would have doubted many of his positive reactions emphasizes the uncertainty surrounding the interpretation of many skin reactions to foods and the value of my elimination method<sup>1</sup> of diet trial for the diagnosis and treatment of food allergy.

Uterine spasms and abnormal bleeding resulting from constitutional reactions from pollen therapy in two patients were first reported by Cooke in 1922.<sup>7</sup> Similar menstrual disturbances were later mentioned by Kahn in 1928<sup>8</sup> and by Robinson<sup>9</sup> in 1929. Thommen<sup>10</sup> recently recorded labor like pains followed by menstruation after a general pollen reaction. Cooke in his original report of such disturbances warned against the danger of abortion from constitutional reactions in pregnancy. These reactions are similar to the gastrointestinal symptoms from pollen therapy reported by Duke,<sup>4</sup> Eyermann<sup>11</sup> and Cohen.<sup>12</sup> I have also observed similar uterine and gastrointestinal symptoms from a constitutional pollen reaction in one patient.

My studies during the last two years have reinforced the fact that food allergy is one cause of menstrual disturbances. Such allergy is most apt to occur in patients who have one or more other allergic disturbances, such as asthma, hay fever, migraine, headaches, neuralgia, cutaneous allergy, or gastrointestinal allergy. Most patients moreover give a positive family history of allergy. However, as with other types of allergy, localization of sensitization in the genital tract may occur without a personal or family history of any other allergy. This necessitates its consideration in the differential diagnosis of all symptoms which are not obviously due to some other cause.

a. Menstrual allergy may produce painful, excessive, scanty or irregular periods. A summary of a previously reported case<sup>1</sup> follows:

CASE 1.—A girl of eighteen years had had extreme pain during the first four hours of her periods for several years. Her bowels had been constipated all her life and for the last three years she had had attacks of pain in the lower right quadrant lasting three or four days, especially before her periods. As a baby she could not tolerate milk, and since then she had never cared for it, though in recent years she had tried to drink it to increase her weight. Her father had severe constipation and hay fever and his father had had asthma. Her mother and the patient's sisters could never tolerate milk. Her physical examination was negative except for an undernourished state and moderate tenderness over the lower right quadrant. No rigidity was found. Roentgen ray studies of her entire gastrointestinal tract were negative except for retarded motility in her ascending colon and moderate lack of mobility in her cecum. Skin tests were negative. With the use of my "elimination diets" her periods have been normal, her constipation has been relieved and no further pain in the lower right quadrant has occurred in the last two years except when milk and wheat have been taken. Definite relief of a lifelong anorexia has resulted.

b. Painful periods accompanied by severe nausea or vomiting which may lead to acidosis may occur due to food allergy. One girl was relieved of painful, excessive periods, long standing constipation, and severe abdominal and bearing down rectal pains before and during bowel movements. This patient moreover was extremely irritable and had recurrent epileptic attacks which were controlled by proper "elimination diets." Such patients may have cyclic vomiting during their childhood before puberty occurs and are subject to migraine after that time. The following case history is of interest.

CASE 2.—A girl aged eighteen had suffered with severe menstrual pains and a scanty flow associated with nausea and vomiting during the last four periods. With the last period these symptoms were extreme and constant nausea and intermittent vomiting had persisted for eight days. There was no personal or family history of allergy. She had refused milk in infancy and had disliked it ever since. However during the last year and especially in the last six months she had forced herself to drink milk to increase her weight. In spite of this, she had lost 10 pounds, her weight being 110 pounds. She had never liked eggs or fish. Her appetite had always been poor. Her physical examination was negative except for a sallow complexion and dehydration from continued vomiting. Skin tests with all types of foods were positive only to shrimp, bass, crab, pepper, and mustard. She was given 500 c.c. of 10 per cent glucose by vein on two successive days which controlled her nausea. Corn meal and rice gruel with pureed vegetables and fruits in "elimination diets" 1 and 2 were then ordered in increasing amounts and within a week she was placed on all foods in "elimination diets" 1, 2, and 3. During the last year her periods have been practically painless and there has been no return of nausea or vomiting except on 2 occasions when moderate cramping and nausea resulted from breaking her diet. Her appetite is better than ever before and her weight is 114 pounds. Wheat, milk, eggs, and fish are still excluded from her diet.

c. Prolonged, abnormal menstruation may be due to food allergy. Bleeding from the intestinal tract and allergic purpura due to food allergy have been reported in the literature<sup>13</sup> and have occurred in my own experience.<sup>1</sup> Moreover allergy should be considered in other types of idiopathic hemorrhage. As I have discussed previously such bleeding is probably due to the increased vascular permeability which is such a characteristic result of allergy. Experimental animals show petechial hemorrhages in various tissues resulting from anaphylactic shock. Thus a woman aged twenty-eight has found that uterine bleeding occurs whenever she eats crab to which no skin reaction occurs. The following case record illustrates this type of allergic bleeding.

CASE 3.—A woman aged thirty had had constant vaginal bleeding between her periods since puberty. One year ago she had several actual hemorrhages. Curettement five years ago gave no help, and in spite of much medical study and therapy, no relief had ever occurred. Marked leucorrhea but no dysmenorrhea was present. Since her earliest memory she had had severe, sick headaches usually two to three times a week. Annoying mental confusion and slowness of thought were frequently present. For two years she had suffered with recurrent urticaria. She had had hay fever in the spring. Moderate bloating, distention, and canker sores had

occurred. Her mother, her maternal aunt, and her grandmother as well as her sister had had migraine. She was not aware of any food idiosyncrasies. She had been married three years and had not been pregnant. Skin reactions were obtained to goose feathers and to a few spring and fall pollens. With "elimination diets" her vaginal bleeding, leucorrhea, urticaria, migraine, constipation, nasal congestion, and her allergic toxemia have been practically absent over a period of six months. Recently she ate a hard boiled egg and two sandwiches which resulted in a severe headache within two hours and vaginal bleeding, which was not associated with a period, on the following morning, lasting two days. Milk, wheat, egg, and chocolate have been found to reproduce her symptoms.

d. Finally leucorrhea may not infrequently be due to food allergy. This allergic reaction was first reported in my recent monograph.<sup>1</sup> Since then Smith<sup>6</sup> has published several other instances of leucorrhea due to food sensitization. I now have records of 9 women in whom leucorrhea was relieved by food elimination. Allergic reactions in the uterine tissues resulting in mucous discharge can be assumed as readily as can similar reactions in the nasal, bronchial, or gastrointestinal membranes. Other allergic disturbances, especially mucous colitis, constipation, and headaches are frequently present in patients with leucorrhea due to food allergy. One patient had had leucorrhea, swelling of her face and of other parts of her body together with a general toxemia for many years due to milk. All of these symptoms returned in a few days with the addition of a few drops of diluted milk to her diet.

The following record illustrates the marked tendency to localization of allergic reactions and the absent skin reactions to allergy producing foods.

CASE 4.—A woman, aged forty, had had eczema behind her ears and in her scalp during childhood. About one and one-half years ago she suddenly developed swelling of her eyelids and cheeks followed by an itching, pigmented, oozing, and scaling eruption extending all over her face. Since then this eruption had been constantly present, being greatly exaggerated for one week before and after each period. For over a year marked leucorrhea associated with severe chafing and sharp burning distress had persisted between her periods. Her eczema had not responded to dermatologic therapy. She had frequent headaches, psychic and physical depression, and lack of energy. Persistent constipation had been present for years. Her physical examination showed the eczematous lesions on her face and a scaling eruption in her scalp. Her blood pressure was 92/70 and marked leucorrhea was present. Her skin tests to all types of food and inhalant allergens by both the cutaneous and intradermal methods were negative. She was placed on "elimination diets" 1 and 2. Her leucorrhea entirely disappeared in two weeks, and her eczema gradually cleared within the first month. She has added diet No. 3 plus potatoes, fish, berries, oranges, melons, and coffee and no return of any of her former symptoms has occurred. Moreover no more depression or lack of energy or "pep" have been present. Her blood pressure is 115/80. If she breaks her diet, immediate constipation, headaches, moderate leucorrhea and a crawling sensation in the skin of her face arise.

Leucorrhea in childhood has been relieved by the elimination of allergy producing foods in 2 patients, indicating that such a cause should be kept in mind when this symptom is present in children.

# OTHER TYPES OF GENITAL ALLERGY

I have previously reported<sup>1, 5</sup> the occurrence of angioneurotic edema in the fallopian tubes as observed by Briggs in 1908.<sup>14</sup> This led to an exploratory operation because of the severity of the pain. Such swellings were also reported by Lyon in 1928<sup>15</sup> in the labia as well as of other regions of the body in a breast fed infant, aged six weeks due to corn and beans in the mother's diet.

CASE 5.—Marked soreness, irritation and excoriation of the vulva due to food allergy were recorded in a previous publication.<sup>1</sup> These symptoms had occurred in a child of seven years since the age of three years. Symptoms were cyclic in nature as are so many allergic conditions. They recurred every few weeks, lasting for two weeks and were associated with a fever of 102-103° F., a marked nasal congestion and a nocturnal cough. Skin tests were entirely negative but with "elimination diets" it was found that milk and wheat were the entire cause of her symptoms. Various physicians previously consulted had never suggested food allergy and had ascribed her symptoms to an acid urine. I have previously stated that much chafing in and around the vulva may also be due to allergy. The occurrence of bladder allergy due to food as described by Duke<sup>16</sup> and myself<sup>1</sup> must be remembered.

## THE INFLUENCE OF MENSTRUATION ON ALLERGIC REACTIONS

It is well known that bronchial asthma, migraine, and other allergic reactions similar to the eczema recorded in Case 4 of this article are precipitated or intensified by the menstrual period. Increased metabolism may be the cause of such exaggeration of symptoms. However, the fact that the elimination of the causative foods prevents the recurrence of the allergic reactions even during the periods, shows that menstruation is not the cause of the symptoms. Thus the termination of periods by means of surgery or radiation therapy is distinctly illogical for the relief of any condition which might be due to allergy and should not be done until thorough testing of the patient with "elimination diets" of various types has been tried. Only recently have I studied two patients whose periods had been terminated unnecessarily and futilely in an attempt to stop migraine. In another patient, hysterectomy on account of a few fibroids was done with the hope that it would eradicate an urticaria. No allergic investigations whatsoever had been made in this woman.

Finally certain marked vasomotor disturbances associated with various allergic reactions are often attributed to ovarian dysfunction. Patients suffering with food allergy may have marked erythema of the face and neck. A woman of sixty years had had swelling of various parts of her body especially of the tongue, face, and hands for two years. Along with these swellings, she had marked flushings of the face and neck which had been ascribed by several physicians to a prolonged menopause. All of her symptoms were relieved with the elimination of wheat and milk from her diet. Thus it may be that so-called "hot flushes" and



other vasomotor disorders at times may be the indirect results of allergy.

#### DIAGNOSIS AND TREATMENT

Careful study of the patient with physical and laboratory examinations must be made so that all existing pathology is discovered. Gynecologic lesions of all types must be carefully ruled out in patients suspected of allergy. However it should be remembered that allergic reactions may accompany other types of pathology.

The determination of the role of food allergy in the etiology of the symptoms of patients suspected of food allergy has been described in my previous publications. Skin tests with all foods and preferably with other types of allergens should be carried out. "Elimination diets"<sup>1</sup> modified by skin reactions to foods as well as by a history of specific food idiosyncrasies should be prescribed. By the gradual development of such diets the allergy producing foods can be discovered.

#### SUMMARY

1. Painful, irregular, scanty, or profuse menstruation may be due to food allergy.
2. Such menstrual disturbances may be associated with severe nausea, vomiting, acidosis, migraine, headaches or other allergic disturbances.
3. Abnormal uterine bleeding and leucorrhea also may result from food allergy.
4. Edema of the tubes, vagina or labia and excoriation and chafing of the labia and of the surrounding skin may arise from food sensitization.

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# SPINAL ANESTHESIA

WITH A REPORT OF 896 CASES\*

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THE renewed interest in spinal anesthesia, in this country as well as abroad, has made it one of the most frequently discussed topics in recent medical literature.

The advantages of spinal anesthesia are numerous, but there are a number of complications which must be duly considered. The most immediate is a slight, moderate, or severe fall in blood pressure. It is usually accompanied by nausea and occasionally vomiting, when the blood pressure falls to about 70 millimeters of mercury or lower. The introduction of ephedrine as a preliminary to spinal anesthesia has helped greatly in diminishing serious results from this complication. H. S. Holder<sup>6</sup> states that the average drop in blood pressure where ephedrine was used was 12.8 millimeters of mercury, when not employed 27.5 millimeters of mercury. In our series, ephedrine was used in every case and the average drop was 21.4 millimeters of mercury.

Until very recently, we gave a hypodermic injection of 0.05 grams of ephedrine preceding the injection of the spinal anesthetic. Blood pressure readings were taken every ten minutes until completion of the operation. When the systolic pressure dropped to between seventy and eighty millimeters of mercury, five minims of adrenalin were given intramuscularly. Recently, we have been giving the ephedrine one-half hour before the injection of the spinal anesthetic and have observed a rise in blood pressure varying from eighteen to forty-five millimeters of mercury in the one-half hour interval; consequently, the fall in the blood pressure following the injection of the spinal anesthetic does not reach as low a level as in the cases which received the ephedrine just preceding the intradural injection and our cases have not required vasomotor stimulation. Also there is less nausea and vomiting because of a lesser fall in the blood pressure.

In our cases where vasomotor stimulation was necessary, we have never seen adrenalin fail to produce a rise in blood pressure. In only one case did we find it necessary to use adrenalin the second time, when we failed to get a response in ten minutes after the first injection. This differs from the experience of McKittrick et al.<sup>7</sup> The reason for the difference in our results may be due to the fact that we use the vasomotor restorative before the systolic pressure becomes very low. We

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have also observed that in our entire series of vaginal operations and in the obstetric cases, where the injection is given in the fourth lumbar interspace, the blood pressure drop was less and did not require vasomotor stimulation. In 10 per cent of our abdominal operations, vasomotor stimulation was used.

Headaches are second in order of complications. The degree varies from a mild sensation of fullness in the head to a severe type of excruciating pain. The occurrence of the headache is due to either a decrease or an increase in the volume of cerebrospinal fluid. Headaches caused by the loss of cerebrospinal fluid are usually noticed when the person tries to raise the head or sit up. Relief is obtained by lying down flat and if persistent, the raising of the foot of the bed will give relief. The application of an ice cap adds to the patient's comfort but coal tar preparations have little or no effect. This type of headache occurred in 5 per cent of our abdominal operations, in 2 per cent of our vaginal operations, and did not occur at all in the obstetric cases.

Headaches caused by an increase in cerebrospinal pressure are much more severe, more difficult to control, and not relieved by position. To reduce the increased cerebrospinal pressure, a retentive enema of six ounces of 50 per cent magnesium sulphate solution may be used with good results and may be repeated at four-hour intervals. When this fails, 2 c.c. of 50 per cent magnesium sulphate solution may be given intramuscularly and as a last resort spinal puncture with the draining off of 10 to 20 c.c. of spinal fluid depending upon the pressure, seldom fails. This type of headache occurred in 0.7 per cent of our abdominal operations, in 0.2 per cent of our vaginal operations, and in none of the obstetric cases. According to various authorities, this complication is caused by introducing blood or foreign substance from the syringe into the cerebrospinal canal, causing irritation, and hence, an increase in cerebrospinal fluid.

With the use of smaller calibre and short bevel spinal puncture needles, which minimizes the trauma to the dura mater, and further improvement in our technic, the number of postoperative headaches has been greatly diminished.

Nausea, and less frequently, vomiting during operation are usually brought about by a marked drop in blood pressure, and in abdominal operations also by pulling forcibly on the mesentery. Idiosyncrasy to morphine sulphate which is given preoperatively may be a contributing cause in some cases. Adrenalin given for the drop in blood pressure usually relieves nausea by causing a rise in blood pressure. A series of deep inspirations on the part of the patient often gives relief. If this is ineffective, inhalation of carbon dioxide and oxygen seldom fails. Nausea alone occurred in 15 per cent of our abdominal operations and vomiting in 6 per cent. In the entire series of vaginal and obstetric operations, the patients did not suffer from this complication.

Nerve injuries may occur following spinal anesthesia. These may manifest themselves in the form of anesthesia, paresthesia, lancinating pains along the course of the nerves, paralysis of motor nerves, and in trophoneurotic changes. However, most of the injuries have been transient, the condition clearing up without leaving any permanent disability. In 1000 cases, Jackson<sup>8</sup> had temporary paresthesia develop in 4. Case,<sup>9</sup> in a series of 1100 cases, reports 1 instance of nerve injury. In our series, nerve injury has occurred twice and both times the same nerve was injured, namely, the abducens. Both cases were unilateral, right-sided, and cleared up very quickly. The onset of symptoms appeared on the third and seventh days respectively. Blatt<sup>10</sup> reviewed the histories of 88 cases and found trochlear nerve involvement in 4 instances and the oculomotor in 6, the remaining 78 involved the abducens; 18 of the 78 were bilateral. The interval between anesthesia and onset of symptoms varied from three days to three weeks. In a large majority of the cases, the paralysis disappeared in from one to three weeks. In a few it lasted from four to nine months and one persisted sixteen months. No satisfactory reason has been established for the selection of the extraocular muscles for this peculiar post anesthetic paralysis. It is to be remembered that the abducens nerve occupies a very superficial position in relation to the fourth ventricle, which later communicates directly through the foramina of Luschka and Magendie with the subarachnoid space into which the anesthetic is injected. In the literature of the last twenty years, 9 cases of meningitis with 2 deaths have been reported. There were none in our series.

One of the foremost advantages claimed for spinal anesthesia is the absence of pulmonary complications. Our experience did not substantiate this claim; we have had 10 pulmonary complications in the first 186 operations.

P. N. Coryllos,<sup>11</sup> in an extensive study on postoperative pulmonary complications and bronchial obstruction, states that of the many etiologic factors of this complication, the diminution in respiratory movement causing a decreased ventilation of the lung, especially the lower lobes, and the consequent formation of mucous exudate, is the greatest.

In spinal anesthesia, respiratory movement is diminished by the inhibition of thoracic and abdominal muscles and by the partial splinting of the diaphragm due to the upward gravitation of the abdominal viscera as a result of the Trendelenburg position, and this in turn permits an accumulation of secretions which become thick, are not absorbed or expectorated, and act as bronchial plugs and are instrumental in producing atelectasis and other forms of pulmonary complications.

After reading the article on "Hyperventilation of the Lungs as a Prophylactic Measure for Pneumonia" by Y. Henderson and H. W. Haggard,<sup>12</sup> we commenced using carbon dioxide and oxygen inhalations for ten minutes at the end of every operation, routinely, with the result

that in the subsequent 710 cases, we have had only 6 cases of pulmonary complications.

P. N. Coryllos<sup>11</sup> also explains the action of carbon dioxide as a prophylactic for postoperative pulmonary complications on the ground that: first, it produces a hyperventilation of the lungs and prevents the deficiency in respiratory excursions which follows anesthesia (especially in abdominal operations), thus providing the alveoli with the necessary amount of air for expulsion of intrabronchial secretions; second, that carbon dioxide by decreasing the hydrogen ion of the exudate, acts upon the pneumococcus to inhibit its growth and probably by favoring the proteolysis of the fibrin in the exudate. Both of these actions have the effect, besides decreasing the virulence of the pneumococci, of the liquefaction of the exudate and its easier expulsion.

As a result of our favorable experience, we advocate the administration of carbon dioxide and oxygen for ten minutes at the end of each operation as a prophylactic measure for postoperative pulmonary complications. As a further prophylactic measure, we postpone operations in the presence of common colds and sinusitis.

The bulk of evidence points to cerebral anemia rather than respiratory paralysis, as the cause of death in spinal anesthesia. According to Koster and Kasman,<sup>5</sup> who have done a great deal of experimental work to confirm this, they state that owing to a marked dilatation of the blood vessels within the abdomen, there is a tremendous fall in blood pressure. The venous return flow to the heart becomes so inadequate that not enough blood can be pumped out to the brain, thus causing a bulbar and cerebral anemia, which is responsible for death.

In reviewing spinal anesthesia and in presenting our experience in 896 cases, we do not desire to convey the impression that this form of anesthesia has all the qualifications of an ideal anesthetic. We do be-

#### STATISTICAL DATA

TABLE I. TYPES OF OPERATIONS

Combined vaginal and abdominal operations on pelvic viscera	311
Abdominal sections for operation on pelvic viscera	167
Appendectomies	56
Cesarean sections	32
Cholecystectomies	24
Cholecystostomies	4
Abdominal section for partial intestinal obstruction	2
Hernias (all types)	26
Nephrectomies	4
Nephropexies	2
Ureterotomy	1
Vaginal plastic operations	141
Vaginal hysterectomies	41
Interpositions	44
Fothergill operations	6
In second stage of labor	35
Total	896

TABLE II. AGE BY DECADES

YEARS	CASES
1 to 9	0
10 to 19	68
20 to 29	229
30 to 39	294
40 to 49	212
50 to 59	76
60 to 69	16
70 to 79	1
Total	896

TABLE III. COMPLICATIONS IN ORDER OF FREQUENCY IN 896 CASES

	629 ABDOMINAL OPERATIONS	232 VAGINAL OPERATIONS	35 OBSTETRIC CASES
Nausea during operation	96	0	0
Drop in blood pressure requiring vasomotor stimulation	62	0	0
Vomiting during operation	38	0	0
Mild headaches due to decrease in cerebrospinal pressure	28	5	0
Severe headaches due to an in- crease in cerebrospinal pressure	5	1	0
Paralysis of abducens nerve	2	0	0

TABLE IV. PULMONARY COMPLICATIONS IN SPINAL ANESTHESIA

(a) In 186 cases before postoperative use of carbon dioxide and oxygen was begun.

	148 ABDOMINAL OPERATIONS	38 VAGINAL OPERATIONS
Lobar pneumonia	1	0
Massive atelectasis	2	0
	(One complicated by lung abscess)	
Bronchitis	5	2

(b) In 710 cases after the use of carbon dioxide and oxygen postoperatively was instituted routinely.

	481 ABDOMINAL OPERATIONS	194 VAGINAL OPERATIONS	35 OBSTETRIC CASES
Lobar pneumonia	1	0	0
Massive atelectasis	1	0	0
Bronchitis	3	1	0

lieve that it has many advantages over other forms of anesthesia and the disadvantages can be greatly diminished by perfection in technic and a thorough understanding of the complications and their treatment. The operating room must be thoroughly equipped and the operating room force trained in assisting to combat these complications.

*Technic.*—All patients receive a preliminary hypodermic injection of morphine sulphate, grain  $\frac{1}{4}$ , scopolamine hydrobromide, grain  $\frac{1}{150}$ , ephedrine sulphate, grain  $\frac{3}{4}$ , one-half hour before operation. Heretofore, we gave the ephedrine and followed immediately with the spinal

anesthesia injection and recently changed to giving it one-half hour before. We find, as I mentioned before, that the blood pressure is better maintained and the drop in blood pressure is less, as shown by diagram.

The drug used is neocaine, the amount varying, depending on the length of time necessary for operation. In abdominal and vaginal operations, we use 100 milligrams; abdominal and vaginal operations combined, 120 milligrams. A flexible, short beveled, 22-gauge lumbar puncture needle is used and the passage of the spinal needle is preceded by an injection of 1 c.c. of 1 per cent novocaine solution subcutaneously and into the interspinous ligament. The fourth lumbar interspace is used in pelvic operations; the third lumbar interspace for abdominal operations below the umbilicus and the second lumbar interspace for other abdominal operations. About 3 c.c. of spinal fluid are collected into the ampule containing the neocaine and after the solution is effected, it is reinjected very slowly without barbotage and the patient is placed immediately in the Trendelenburg position. Care is taken not to lose any cerebrospinal fluid when adjusting the syringe to the needle, as this tends to diminish the pressure in the cerebrospinal canal and allows for greater diffusion of the liquid.

Blood pressure readings and the pulse rate are recorded every ten minutes and if the systolic pressure drops to between 80 and 70 millimeters of mercury, five minims of adrenalin are given intramuscularly. The greatest drop in blood pressure usually occurs in the first fifteen to twenty minutes. The drop in blood pressure in vaginal and obstetric operations in our series was very slight and required no vasomotor stimulation. At all operations hypodermoclysis apparatus and normal saline solution are always ready for immediate use and can be administered in two minutes from the time the order is given. This is reserved for cases in which the blood pressure continues to drop in spite of vasomotor stimulation; when the blood pressure falls to 35 millimeters of mercury, the degree of the Trendelenburg position is increased and an intravenous injection of saline with one drop of 1:1000 adrenalin chloride solution to every 100 c.c. of saline, as advocated by Babcock,<sup>4</sup> is administered. In our series, we used this procedure once in a fatal case which I will report in detail.

The duration of anesthesia is variable. It can be depended upon from three-quarters to one hour in abdominal operations and one to one and one-quarter hours in vaginal operations. Unknown factors as well as amount of neocaine used determine the duration of anesthesia. In our series, we used supplementary anesthesia 68 times in 629 abdominal operations, or about 10 per cent, and in 3 per cent of our 232 vaginal operations and none in the 35 obstetric cases. The supplementary anesthetic used in most cases was nitrous oxide and oxygen and lately we have been using ether, open drop method. If the operation itself has

been completed, the abdomen can be closed by injecting 1 per cent solution of novocaine locally.

Failure to obtain anesthesia is due to faulty technic, in making the injection extradurally or pushing the needle in too far between the fibers of the cauda equina into the anterior compartment which results in but little of the anesthetic fluid reaching the posterior compartment. This occurred in 3.5 per cent of our first 362 cases and 0.9 of 1 per cent in the remaining 534 cases, showing a decrease in failures with increase of experience and improvement in technic.

I wish to report at this time, in detail, the one death which occurred in our series during the operation under spinal anesthesia.

#### CASE REPORT

Female, fifty-five years old, multipara; menopause established at age of thirty-four. Her chief complaints, on admission, were a bloody vaginal discharge for the past three months and a severe vaginal hemorrhage two weeks before admission.

She gave a history of chronic bronchitis and asthmatic attacks for thirty years. Blood pressure, systolic 140, diastolic 80, pulse 80, respirations 24, temperature normal. Urea nitrogen 12, blood sugar 110, Wassermann negative and her urine and blood count were normal.

Upon physical examination the entire chest was hyperresonant, coarse and fine moist râles were audible over the entire chest, the heart was enlarged to the right, sounds were distant, and there were no murmurs. The liver was enlarged downward two fingerbreadths below the costal margin. A spherical, freely movable mass, the size of a grapefruit was palpable in the lower abdomen. Upon vaginal examination, the perineum was relaxed, the cervix was lacerated but well healed, the uterus was enlarged to the size of a three months' pregnancy; it was in the anterior position, freely movable, irregular in outline; there was no induration in the broad ligaments or in the adnexal regions.

A diagnosis was made of multiple fibroma of the uterus undergoing malignant degeneration; chronic bronchitis and chronic myocarditis.

Under nitrous oxide and oxygen anesthesia, a diagnostic dilatation and curettage was performed and typical degenerated carcinomatous tissue removed; these findings were further substantiated by the pathologist as adenocarcinoma of the body of the uterus.

Two days later a panhysterectomy was undertaken under spinal anesthesia. Morphine sulphate, grain  $\frac{1}{4}$ , atropine sulphate, grain  $\frac{1}{150}$ , were given half hour before and ephedrin, grain  $\frac{3}{4}$ , hypodermically a few minutes before the injection of 120 milligrams of neocaine dissolved in 3 c.c. of spinal fluid into the third lumbar interspace. The patient was immediately placed in the Trendelenburg position.

The systolic blood pressure dropped to 90 millimeters of mercury in the first twenty minutes and rose to 130 millimeters of mercury ten minutes later. In forty minutes after the injection, the blood pressure was 135/70; pulse 90 per minute and of good volume. Patient began to complain of pain, whereupon nitrous oxide and oxygen were given for fifteen minutes, at which time the operation was completed and the closure of the abdomen was in progress, when suddenly, she became pulseless, respiration became shallow, and the heart sounds were not audible. The Trendelenburg position was increased, intracardiac injections of adrenalin were administered, intravenous injections of saline and adrenalin were started; caffeine, sodiobenzoate and camphor were given; artificial respiration was attempted but there was no response.



Permission was not obtained for a postmortem examination. In analyzing this case, we believe that in view of the bronchitis and myocarditis of such long standing, spinal anesthesia was the anesthetic of choice. Forty minutes after the injection of the spinal anesthesia, when the nitrous oxide and oxygen were started, her systolic pressure was 135, diastolic 70. Therefore, the possibility of complications from spinal anesthesia was passed, because usually such complications occur within twenty minutes, seldom thirty minutes after the injection. The first sign of trouble was absence of pulse and heart action rather than respiration, which, though feeble, continued. Upon these facts, we base our conclusion that this was a cardiac death due to the poor selection of nitrous oxide and oxygen as an auxiliary anesthetic rather than to the spinal anesthetic.

#### SPINAL ANESTHESIA IN THIRTY-FIVE OBSTETRIC CASES

Gravocaine, a heavy solution for spinal anesthesia, (manufactured by Metz & Co., according to Pitkin's formula) was used to terminate the second stage of labor in thirty-five cases.

The advantages claimed by Pitkin<sup>13</sup> for this form of anesthesia over ordinary spinal anesthesia were substantiated in our series. We found, as he claims, that it does not affect normal uterine contractions; that the drop in blood pressure is very slight or absent, and that there is no nausea, vomiting, or headaches. It has the further advantage over inhalation anesthesia, in that it produces extreme relaxation of the soft parts and a rigid or spasmodic cervix can be dilated manually; forceps can be applied with greater ease, and there is less trauma to the cervix and pelvic floor.

The anesthetic is injected into the fourth lumbar interspace and one or two drops of spinal fluid aspirated to make certain that the needle is not displaced. The semireclining or reverse Trendelenburg position is assumed and maintained for two and a half to three hours in order to avoid possibility of having the anesthetic ascend in the canal. The anesthesia lasts for forty-five or sixty minutes, sufficient time for forceps operation or perineal repair, if necessary, making supplementary anesthesia unnecessary.

In our series, the usual fall in blood pressure accompanying spinal anesthesia, was entirely absent in 20 cases and in the remaining 15 cases, the drop was so slight that no vasomotor stimulation was necessary. Nausea, vomiting, headaches, and pulmonary complications were absent.

In all the babies born, breathing was established at birth.

There were 20 low or outlet forceps deliveries. Kielland forceps were used 10 times for occipitoposterior positions and 5 times for deep transverse arrest of the head. Twenty-seven of the women delivered were primiparae; 8 were multiparae; episiotomy was performed 20 times.

#### SUMMARY AND CONCLUSIONS

1. Carbon dioxide and oxygen administration is a valuable prophylactic against pulmonary complications developing in spinal anesthesia,

as shown in our cases. When no carbon dioxide and oxygen were used, we had 5 per cent of pulmonary complications; when carbon dioxide and oxygen were used, 0.8 of 1 per cent developed pulmonary complications.

2. The preoperative use of ephedrine, especially if given half hour before the spinal anesthetic, is a good prophylactic against too great a drop in blood pressure and its sequelae. The preoperative use of ephedrine has eliminated low blood pressure as a contraindication for the use of spinal anesthesia.

3. Adrenalin as a vasomotor stimulant during spinal anesthesia has not failed in our experience, but in order to get good results, it must be given early, before the blood pressure drops to too low a level. Best results are obtained if the adrenalin is given when the systolic pressure drops between 80 and 70 millimeters of mercury.

4. Our experience with gravocaine, a heavy solution of spinal anesthesia, in a small series of obstetric cases has been most satisfactory in every way.

5. The disadvantages of spinal anesthesia can be greatly diminished by perfection in technic, a thorough understanding of the complications and their treatment and by having the operating room equipped and the operating room force trained in assisting to combat these complications as soon as they arise.

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2106 SPRUCE STREET.

(For discussion, see page 440.)

**Obadalek: Twisted Ovarian Cysts in Childhood.** Monatschr. f. Kindhk. 48: 419, 1930.

The author reports four cases of twisted ovarian cysts in little girls, aged from two to ten years. The clinical picture is very similar to an acute appendicitis. The differential diagnosis is based on the following points: Onset with very severe pain, and appearance of peritoneal symptoms somewhat later. There is marked tenderness of the Douglas sac. A tumor can be found in the abdomen. There is an early disturbance in emptying of the bladder.

The treatment must be surgical. The prognosis is rather favorable. The mechanism of the twisting is different from that seen in adults, and especially in younger children. The most important factor seems to be the filling of the bladder. If this reaches extreme degrees it may lead to a torsion of the cyst. The reasons for this process are the more cranial position of the ovaries in children and also the size of pelvis and of womb. Occasionally, other mechanisms may lead to a torsion.

ZENTAY.

## FURTHER STUDIES ON TRICHOMONAS VAGINALIS (DONNÉ)\*

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IN A former communication on *Trichomonas vaginalis* we reported the results of cultural studies of patients in whom the flagellates were found in large numbers in the vaginal discharge.<sup>1</sup> We described the clinical picture of the vaginitis with the parasite, and two new media which we had developed for the successful cultivation of the organism. Seventy-six clinical cases were reported up to September, 1930, with cultural studies both by aerobic and anaerobic methods in 26. Many of these cultures, taken in the summer and fall of 1930, have been successfully carried through the entire winter and spring. For example, one of our strains was isolated in July, 1930, and in July, 1931, was *still living in its ninetieth subculture*. Another strain isolated in October, 1930, survived up to July, 1931, through more than seventy subcultures. A number of different strains were isolated each month through the winter and spring of 1930-31 and were kept alive in artificial culture media until late in June, 1931, when, due to the pressure of other work, they were discarded. This is contrary to the experience of Davis<sup>2</sup> and others who report an apparent seasonal variation with inability to culture fresh or to carry previously isolated strains through the late winter and early spring months. Davis, however, in a recent personal communication reports the successful culturing of the parasite at all seasons.

The effect of heat and cold on the survival of *Trichomonas vaginalis* was indicated on two occasions when the incubator was down to 25° C. for forty-eight hours. The cultures were apparently killed, as no motile trichomona were seen on hanging-drop examination; nevertheless, subcultures revealed living trichomona. On the other hand, at another time the temperature of the incubator rose to 40° C. for thirty-six hours. Five of the seven strains were killed by the heat, two of which had withstood the previous chilling. Repeated subcultures from these five failed to grow.

Examination of fresh warm stools from a number of patients with *Trichomonas vaginalis* vaginitis did not show the presence of either *Trichomonas vaginalis* or *Trichomonas hominis*. This is in accord with our previous findings and has been verified by Bland et al.,<sup>3</sup> and by Kleegman who found no flagellates in the rectum in a series of 78 cases.<sup>4</sup>

The pathogenicity of *Trichomonas vaginalis* is questioned by many gynecologists as well as parasitologists. It is the belief of many that the purulent discharge is the result of specific bacterial infection of the vagina and that the *Trichomona* enter merely as secondary invaders.

\*From the Albert Kuppenheimer fund of the Michael Reese Hospital and Nelson Morris Institute for Medical Research. Read before the Chicago Gynecological Society, November 20, 1931.

Others believe that the primary pathogene is a yeast and that the trichomona occur symbiotically as a nonpathogenic parasite.

Plass<sup>5</sup> reports a series of cases in which the monilia and Trichomona were found either alone or in combination. He attributes the clinical symptoms to the presence of monilia and regards the Trichomona as a probable secondary invader of little pathogenic importance.

Curtis<sup>6,7</sup> in a comprehensive study of the bacteriology of vaginal secretions, established the following bacterial flora. In vaginal secretions from patients without clinical symptoms, he reported a predominance of Döderlein bacilli associated with various other organisms in small numbers; in cases with a purulent discharge, Döderlein bacilli, an anaerobic gram-negative bacillus, and a gram-positive diplococcus predominated with a great variety of other organisms in varying numbers. The diplococcus found consistently was sometimes oval and sometimes lancet-shaped on direct smear examination, and chained when grown in artificial culture media. Less frequently he found *B. coli*, a gram-negative diplococcus other than the gonococcus, staphylococcus, and diphtheroids. All of these organisms proved nonpathogenic for the common laboratory animals in which Curtis injected both vaginal washings and cultures of the organisms.

#### FURTHER INVESTIGATION

In order to establish the true rôle of *Trichomonas vaginalis* in the typical clinical condition which is well recognized today as *Trichomonas vaginalis* vaginitis, we continued our studies with particular attention to the associated bacteriology of the vagina in *Trichomonas* vaginitis and also the possible rôle of the yeasts. In the following series of cases, we studied office patients, private and service hospital patients, and out-patients from the Mandel Clinic of the Michael Reese Hospital in order to obtain a representative group. More material was obtained from private patients than from the clinic, however, because in our experience during the past two years, we have noted that this type of vaginitis is far more frequently found in private clientele than in service cases. Twenty-two patients suffering with typical *Trichomonas vaginalis* vaginitis, and 31 patients in whom there was no clinical or laboratory evidence of *Trichomonas vaginalis* were selected. No douching or other local treatment was permitted for one week prior to examination. The diagnosis of trichomonas was first confirmed by fresh hanging-drop examination and then cultures were made. Material for trichomonas cultures was removed from the vaginal vault by means of a sterile pipette, using a sterile bivalve speculum. The vaginal secretion was placed in a test tube containing about 4 c.c. of placenta broth (described in our first publication) for transportation to the laboratory. One half of the suspension in placenta broth was then transferred to each of the two media used for culture; namely, blood-agar slants, and placenta-agar slants, each covered with Locke's solution containing 5 per cent human blood serum. Hanging-drop examination of these cultures was made at the end of twenty-four hours and if negative, again at the end of forty-eight hours, incubation for the presence of living *Trichomonas vaginalis*. In every case in which trichomonas, were found in the direct examination by the

TABLE I

	T. VAGIN- ITIS. FLAG- ELLATES PRESENT	TREATED CASES. NO TRICH- OMONAS WHEN CULTURED	T. VAGIN- ITIS IN PREGNANCY	NORMAL PREGNANCY NO TRICH- OMONAS	POSTPARTUM 12 DAYS. POS- ITIVE TRICH- OMONAS BE- FORE AND AFTER LABOR	POST- PARTUM 11 DAYS. NEG. TRICH- OMONAS	POST- PARTUM 13 DAYS. CE- SAREAN. NO TRICH- OMONAS	LEUCOR- RHEA; NO TRICH- OMONAS	POSTOPERA- TIVE (1 WEEK). DILATATION AND CU- RETTAGE	NORMAL; NO LEUCOR- RHEA	VIRGIN; NO PELVIC PA- THOLOGY
No. of cases	17	5	5	11	2	1	1	8	1	7	1
Döderlein bacil- lus	15	5	4	9	2	1	1	7	1	5	1
Large gram-pos. nonhemolytic streptococcus	17	5	5	11	2	1	1	6	1	6	1
Lanceet-shaped gram-pos. non- hemolytic streptococcus	3	1	2					1		1	
Large gram-pos. hemolytic strep- tococcus								1		1	
Small gram-neg. nonhemolytic streptococcus	3	1									
Small gram-neg. diplococcus (not gonococ- cus)	2					1					5
Staphylococcus	1			1							

TABLE I—CONTINUED

	T. VAGINITIS, FLAGELLATES PRESENT	TREATED CASES. NO TRICHOMONAS WHEN CULTURED	T. VAGINITIS IN PREGNANCY	NORMAL PREGNANCY NO TRICHOMONAS	POSTPARTUM 12 DAYS. POSTITIVE TRICHOMONAS BEFORE AND AFTER LABOR	POSTPARTUM 11 DAYS. NEG. TRICHOMONAS	POSTPARTUM 13 DAYS. CE-SAREAN. NO TRICHOMONAS	LEUCORRHEA; NO TRICHOMONAS	POSTOPERATIVE (1 WEEK). DILATATION AND CURETTAGE	NORMAL; NO LEUCORRHEA	VIRGIN; NO PELVIC PATHOLOGY
<i>B. coli</i>	3	1	3	1	2		1	3	1		
Gram-neg. bacillus, (not colityphoid group)	8		1					5	1	7	
Very thin gram-neg. bacillus ( <i>Vibrio</i> )	1	1		2					1	1	
Large gram-neg. spore-bearer	2										
<i>B. mucosus</i>	1	1						1			
Small gram-pos. bacillus	3							1		2	
Diphtheroids	3	1		2		1			1	1	
Sarcinae	1										
Yeasts	1	1	2					1			
<i>Trichomonas vaginalis</i>	17	0	5	0	2	0	0	0	0	0	

hanging-drop method we were able to cultivate the flagellates artificially. Conversely, in no case were we able to demonstrate the presence of trichomonas by cultural methods when they could not be found in the original hanging-drop examination. The latter was noted also in the study made by Bland, Goldstein, and Wenrich.<sup>3</sup>

Material for the bacteriologic determinations was obtained by using sterile swabs, and direct smears were made in each instance. Aerobic cultures were made in ascites veal infusion broth P<sub>11</sub> 7.6, on streaked blood-agar plates, and on endo-agar plates. These were examined after twenty-four hours' incubation. A streaked blood-agar plate was incubated for three days in a McIntosh and Fildes's anaerobic jar and then examined. Maltose agar slants (4 per cent) were also streaked and incubated at room temperature for three days to ascertain the presence of yeasts. All smears were stained by Gram's method.

Direct smears were carefully examined for gonococci but in no instance were they found. Varying reports have been published as to the frequency of finding both gonococci and *Trichomona vaginalis* in the same patient. The large majority of workers did not observe this dual infection; those who did, report it in a very small percentage of their cases.

#### CULTURE STUDIES (TABLE I)

Seventeen patients showing the typical clinical picture commonly recognized as *Trichomonas vaginalis* vaginitis, with actively motile trichomona in the vaginal discharge, presented a varied bacterial flora; large gram-positive nonhemolytic streptococci were present in all cases, and Döderlein bacilli in all but two. Among other organisms found in a smaller proportion of the cases were a small nonhemolytic gram-negative streptococcus, a small gram-negative diplococcus (not gonococcus), staphylococcus, *B. coli*, gram-negative bacillus not of the typhoid-coli group, a very thin gram-negative bacillus (*Vibrio*), large gram-negative spore-bearer, *B. mucosus*, small gram-positive bacillus, and diphtheroids. Yeasts and sarcinae were found in only one case each.

In a group of 5 patients who had *Trichomonas vaginalis* vaginitis complicating pregnancy, gram-positive nonhemolytic streptococci were found in all cases and Döderlein bacilli in all but one. A small gram-negative nonhemolytic streptococcus, staphylococcus, *B. coli*, and a gram-negative bacillus not of the typhoid-coli group were found less frequently. Yeasts were seen in only 2 cases.

Two cases were selected with *Trichomonas vaginalis* vaginitis complicating pregnancy for cultural studies before and after delivery (twelve days postpartum). The bacteriology in the 2 cases was identical both before and after delivery: gram-positive nonhemolytic streptococcus, Döderlein bacilli, and *B. coli*. *Trichomonas vaginalis* were present in all examinations. In one of these 2 cases yeasts were present before but not after delivery; in the other one no yeasts were found.

In the group of 5 patients, who had previously had *Trichomonas vaginalis* vaginitis but who were apparently free of the parasite at the time of taking the cultures, Döderlein bacilli and gram-positive nonhemolytic streptococci were present in all cases. A small gram-negative nonhemolytic streptococcus, *B. coli*, thin gram-negative bacilli (*Vibrio*), *B. mucosus*, and diphtheroids were found in various proportions. In one case yeasts were present.

In a group of 11 patients who were pregnant and did not harbor the flagellate, gram-positive nonhemolytic streptococci were recovered in all cases, and Döderlein

bacilli in 9 cases. The other organisms found were a very thin gram-negative bacilli (*Vibrio*), diphtheroids, and *B. coli*. No yeasts were found.

One patient was examined eleven days after a normal delivery, with no evidence of trichomonas infection. Gram-positive nonhemolytic streptococci, Döderlein bacilli, and diphtheroids were obtained on cultures.

Cultures from the vagina in one patient, who had had a cesarean operation and subsequently an abdominal wall abscess, but with no evidence of *Trichomonas* vaginitis, were taken twelve days postpartum. The organisms found were gram-positive nonhemolytic streptococci, Döderlein bacilli, and *B. coli*.

Vaginal cultures were taken from another patient one week after dilatation and curettage. No trichomonas were present. Gram-positive nonhemolytic streptococci, Döderlein bacilli, *B. coli*, gram-negative bacillus not of typhoid-coli group, thin gram-negative bacilli (*Vibrio*), and diphtheroids were found.

An adult virgin with no evidence of pelvic pathology yielded only three types of organisms upon culture: gram-positive nonhemolytic streptococci, the Döderlein bacillus, and *B. mucosus*.

Eight women with profuse leucorrhea without trichomona were selected for study. Gram-positive nonhemolytic streptococci were found in all cases and Döderlein bacilli in all but one. In addition, small gram-negative bacilli not of the typhoid-coli group, *B. coli*, a small gram-negative nonhemolytic streptococcus, *B. mucosus*, and a small gram-positive nonhemolytic streptococcus were found in various proportions in the group. In only one case were yeasts recovered.

Seven patients with normal vaginal status (without leucorrhea) were also used as a set of control cases. A gram-negative bacillus not of the typhoid-coli group, was present in all instances. Large gram-positive streptococci were seen in 6 cases, and Döderlein bacillus and staphylococcus in 5 cases. Other organisms found in a small number of the cases were a large gram-positive hemolytic streptococcus, a small gram-negative diplococcus (not gonococcus), a very thin gram-negative bacillus (*Vibrio*), a small gram-positive bacillus, and diphtheroids. No yeasts were found.

#### SUMMARY

The cultures confirmed the findings of direct smear examinations although the relative number of the various organisms was affected by culturing. Döderlein bacillus grows very scantily, and the gram-positive nonhemolytic streptococcus cultures luxuriantly. No group of strict anaerobes was found, although the gram-positive streptococcus and the gram-negative bacillus grew readily under anaerobic as well as aerobic conditions. The only organisms found with any degree of consistency in all patients with *Trichomonas vaginalis* vaginitis were the Döderlein bacillus and the gram-positive nonhemolytic streptococcus. These organisms were likewise found in about the same proportions in all cases in which no *Trichomonas vaginalis* were found. The streptococcus, in agreement with the experience of Curtis, appeared in a diplococcic form in direct smear examination and was either oval or lancet-shaped. It formed chains when grown on artificial culture media.

A number of streptococci isolated from our cultures were subcultured in sugar (lactose, mannite, salicin, and saccharose) and according to Holman's<sup>9</sup> classification, belonged to the following groups: *Streptococcus ignavus*, *Streptococcus salivarius*, and *Streptococcus nonhemolyticus* III. Other bacteria found less consistently in both groups were *B. coli*,



a staphylococcus, *B. mucosus*, diphtheroids, a small gram-negative diplococcus (not gonococcus), a small gram-negative bacillus not of the typhoid-coli group, a thin gram-negative bacillus (*Vibrio*), a large gram-positive spore-bearer, and one large gram-positive hemolytic streptococcus. No cases with gonorrheal infection were found among the group with *Trichomonas vaginalis* vaginitis and none were used for control cases.

Direct smear examination, verified by cultures, revealed the presence of yeasts in only 6 of our 59 patients. One of these had *Trichomonas vaginalis* vaginitis; another had a previous history of trichomonas, but she was apparently cured; 2 had *Trichomonas vaginalis* vaginitis complicating pregnancy; and 1, who showed no evidence of trichomonas infection, had a profuse leucorrhea. It is apparent from this study that yeasts were not responsible for the vaginitis in the group of women under our observation. It is also obvious that inasmuch as the same group of bacteria was found in the vaginal secretion in the presence of *Trichomonas vaginalis* as in that without the parasite, the flagellate is responsible for the altered clinical picture.

From our clinical and laboratory studies of more than one hundred cases of *Trichomonas vaginalis* vaginitis over a period of approximately eighteen months, we believe the following conclusions may be drawn:

#### CONCLUSIONS

1. No specific or altered bacterial flora was found to be responsible for the purulent vaginitis in this group of women with *Trichomonas vaginalis* infection. The same organisms were found associated with the trichomonas as are found in health and in ordinary leucorrhea.

2. Gonococci were not found associated with trichomona in any of our patients. Many of the control group suffered from chronic endocervicitis which may have been caused originally by gonorrhea, but in these we failed to find trichomona. *Trichomonas vaginalis* vaginitis, however, frequently follows a gonorrheal infection.

3. The presence of *Trichomonas vaginalis* in large numbers in the vagina accompanied by a purulent discharge is responsible for the distressing symptom complex recognized as *Trichomonas vaginalis* vaginitis.

4. *Trichomonas vaginalis* is pathogenic for human beings under certain clinical conditions.

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## HYSTEROSALPINGOGRAPHY IN STERILITY STUDIES\*

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**H**YSTEROSALPINGOGRAPHY was first attempted by Cary in 1914. He used a solution of collargol to inject the pelvic organs and followed this by roentgenograms. Other investigators worked along these lines but on account of the marked peritoneal reaction which invariably happened whenever collargol entered the peritoneal cavity this method was soon discarded.

In 1920 Rubin published his great contribution containing the results of his first transuterine tubal air inflation, now known as the "Rubin test." This method was soon combined with x-ray examinations for the demonstration of the pelvic organs, and known as transuterine pneumoperitoneum. Other observers combined the transabdominal and transuterine gas inflation in many cases to distinct advantage and contributed much to the perfection of gynecologic roentgenography.

Notwithstanding the great assistance given the diagnostician by the pelvic pneumoperitoneum there was a slowly gaining impression that the Rubin test had not entirely solved the problem of exactly determining the patency of the fallopian tubes. Many investigators reported the use of various other radiopaque substances in their efforts to find a satisfactory and safe medium. However, it was not until the general use of an iodized oil that the problem entered the stage of its final solution. Sicard and Forestier in using lipiodol, a preparation made by L. Lafay, in the form of intramuscular injections for the treatment of diseases in which a slow prolonged iodine medication was desired, accidentally discovered that this substance casts excellent shadows on the roentgenograms. They also observed the fact that it was entirely harmless and perfectly tolerated by the patients. These investigators began immediately to inject various body cavities for x-ray diagnosis. It is an interesting fact that despite this very detailed investigation that followed, in the report given before the Société Médicale des Hôpitaux de Paris in 1922, Sicard and Forestier failed to mention its use in conjunction with pelvic roentgenography. It was Heuser of Buenos Aires, in 1921, who obtained the first roentgenogram of the uterine cavity injected with lipiodol. His observations were reported in 1924.

Since that time the literature has been filled with articles concerning the various phases of the gynecologic application of lipiodol. Iodized oil seems to have stood the test. Because of the high iodine content, it is impervious to the roentgen rays. It is self-disinfecting and mildly germicidal, two very important factors.

Hysterosalpingography, therefore, today stands as an accepted prac-

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tical method of diagnosis and deserves a place in the diagnostic armamentarium of every gynecologist. Just as the Rubin test has gained a permanent place in the orderly investigation of the childless woman, so the hysterosalpingogram has a place of its own. When the test for tubal patency is indicated, the method of choice is the Rubin test with carbon dioxide under manometric control. If unsatisfactory and unconvincing

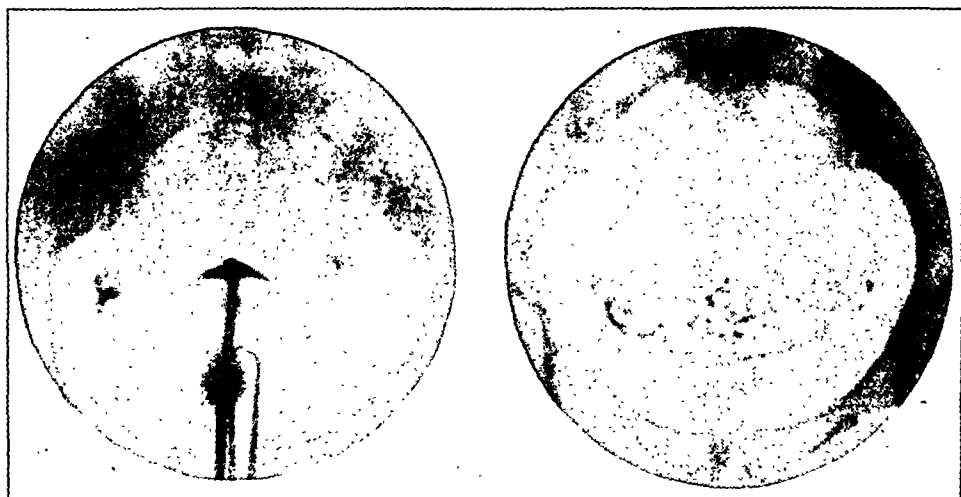


Fig. 1.—Infantile uterus with patent tubes.

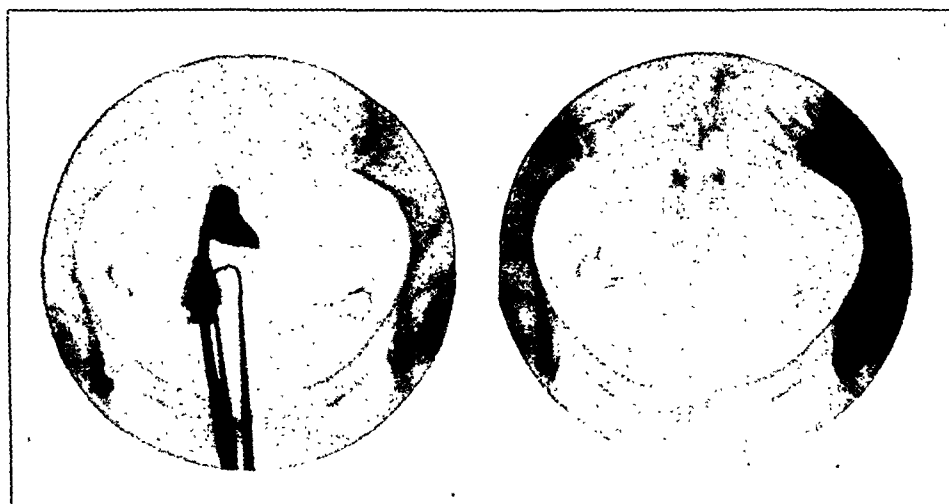


Fig. 2.—Hyperplasia endometrium, retroversion uteri and patent tubes.

results are obtained in testing tubal patency and when a permanent diagnostic record is desired, supplementary methods employing iodized oil and x-rays, should be employed. The filling may be observed fluoroscopically, and definite shadows on a permanent record are made which show the "spill" into the peritoneum or not as the case may be.

It is the policy of the sterility clinic at the Hospital of the Woman's

Medical College of Pennsylvania to consider the use of hysterosalpingography in:

1. All cases with patency of the fallopian tubes where the Rubin test, the palpatory findings, or other diagnostic methods employed in investigation have failed to furnish satisfactory explanation of the cause of sterility.

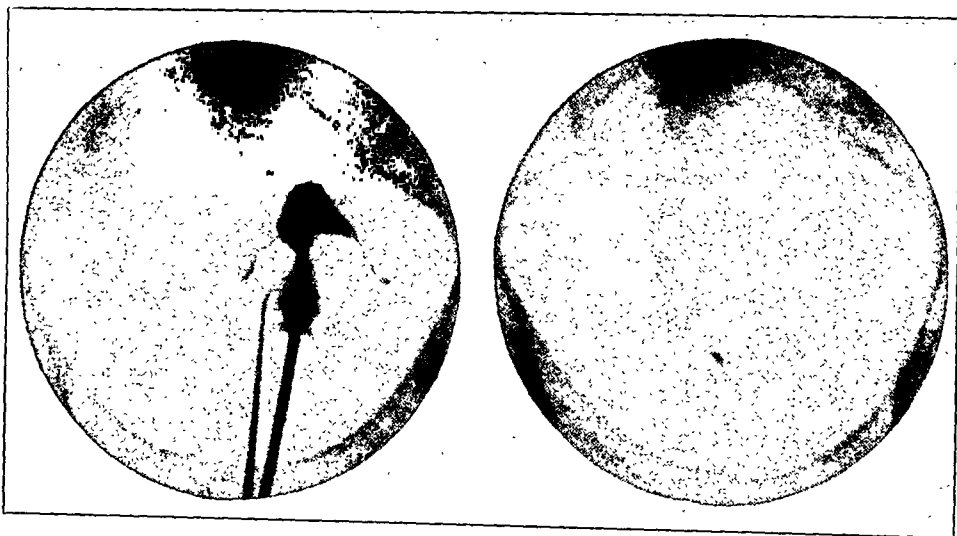


Fig. 3.—Fimbriated occlusion of the tubes.

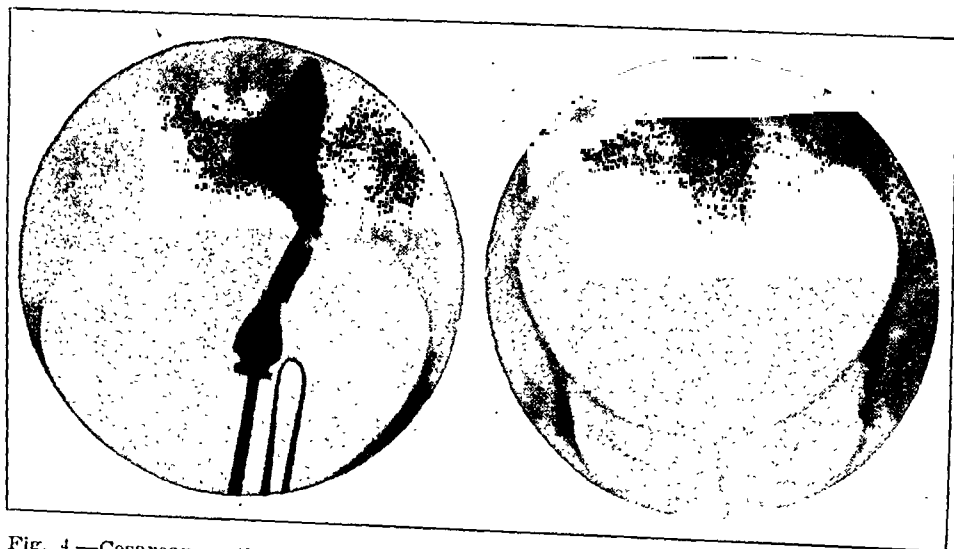


Fig. 4.—Cesarean section nine years ago. Cornual occlusion and subinvolution uteri.

2. All cases of tubal occlusion as demonstrated by a previous Rubin test, for determination of:

- a. Whether the occlusion of the tubes is unilateral or bilateral.
- b. Location of occlusion.

The patient to be examined reports at the hospital on the fifth to seventh day following the last day of her menstrual period. A mild

laxative, preferably compound licorice powder, is ordered the night before. An enema and douche are given after arrival at the hospital. No preliminary opiates are necessary as a rule, because the discomfort is only slightly more than experienced by the Rubin test. With all our cases a cannula with the rubber olive attachment to plug the cervix, a mercury manometer, and French lipiodol heated to about 100° F. are

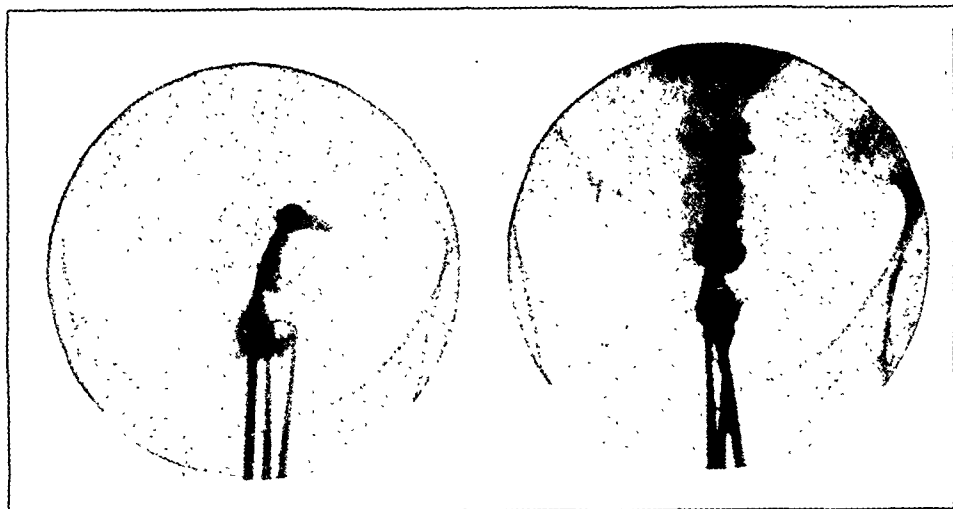


Fig. 5a.—Partial occlusion. Left tube patent.

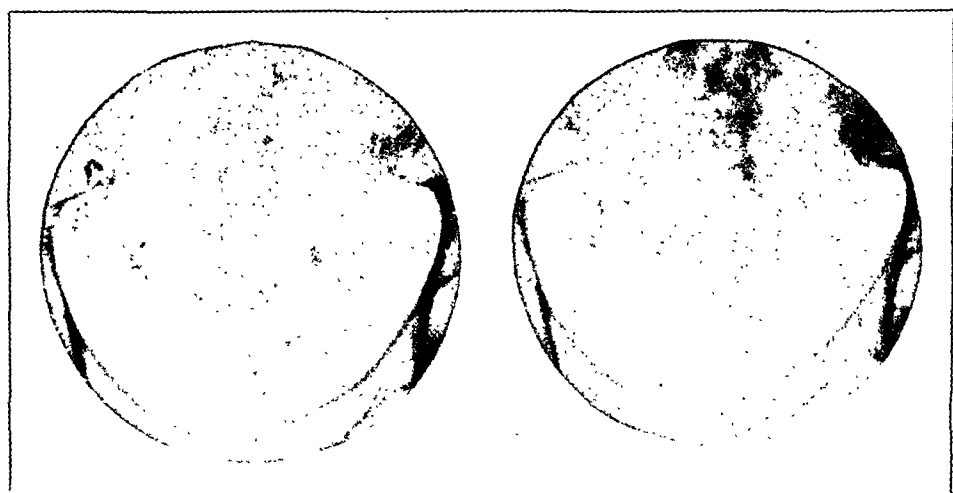


Fig. 5b.—Right tube opened patently.

used. The technic employed is not dissimilar to that used by others. The normal uterine cavity has been found to have a capacity of about 2 c.c. to 4 c.c. of oil and after slowly injecting that amount the pressure is watched while more oil is injected. The amount of oil necessary to fill the normal uterine cavity and the tubes averages around 4 c.c. If after injecting 4 c.c. of lipiodol the pressure of the mercury has not reached two hundred, a film is taken to be sure that enough oil has been used. It

is desirable not to allow too much oil to spill into the peritoneum. However, we must be sure that we are not dealing with a very large uterine cavity and, hence, need more oil to fill the tubes. The pressure indicated by the mercury manometer is never allowed to rise above two hundred. Serial films are often necessary to demonstrate conclusive findings. As a rule, the routine with us is to take one or more films at the time of injection and again at the end of six hours and twenty-four hours. A douche is given preliminary to the six- and twenty-four-hour roentgenograms to wash out any oil that has been expelled into the vagina.

The shadows cast give information (1) as to the shape, relative size, and position of the uterine cavity (Figs. 1, 2, and 4), (2) as to whether the tubes are patent or occluded (Figs. 1, 3, 4, 5a, 5b, and 6).

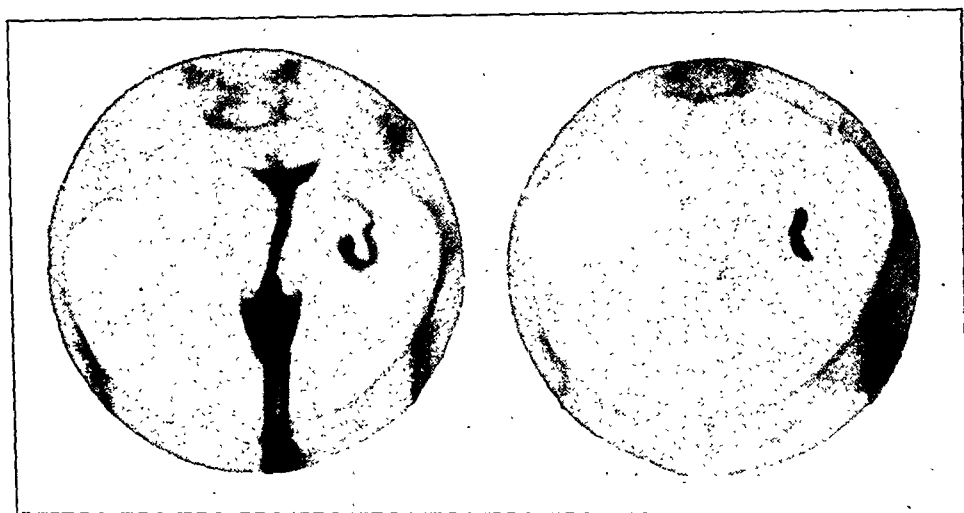


Fig. 6.—Fimbria of the right tube occluded. Partial cornual occlusion of the left tube.

The changes in position of the uterine cavity, which as a rule are due to malposition of the uterine body as a whole, are recognized in the majority of cases by clinical manipulation. Hence, to demonstrate them by means of the injection of opaque media, is for academic interest purely. But the changes in size and shape are of great value if visualized. Considering that a large number of sterilities are due to developmental anomalies not always easily diagnosed palpably, the roentgenogram furnishes great aid. The infantile uterus is a most common example and will demonstrate itself by its small capacity in holding only about 0.5 c.c. of oil and casts a very small triangular shadow.

If the tubes are patent, information is gained as to whether one or both are open and also whether one or both opened during the test. This latter observation is concerned with whether the spill occurs at once or is observed subsequently in the six- or twenty-four-hour roentgenograms. If the tubes are occluded, information is discovered as to the location of the obstruction. Hence, the type of operation necessary to open the tubes may be determined upon prior to the operation.

We must not overlook a third advantage of the injection of lipiodol for salpingography, the not infrequent therapeutic effect. Repeatedly in the literature mention is made of finding the tubes open after one or more lipiodol injections. Jarcho reports a case of bilateral tubal occlusion which ten months later showed a normal picture.

After all, the success in sterility therapy lies in the subsequent pregnancy with delivery of a full-term child. Witmer, Cushman, and Leucutia in their search of the literature to February, 1930, found 25 cases reported of pregnancy following the use of uterosalpingography in sterility studies of cases with occluded tubes. In August, 1931, Robbins and Shapira reported that "of one hundred and thirty-three cases, in which one or both tubes were found to be or caused to be patent by injection of lipiodol, thirty-two became pregnant." What other factors might have been contributory to results in their series are not stated.

However, sufficient success has followed to emphasize the importance of hysterosalpingography in sterility study and therapy. We wish to report one case which to us points very definitely to success following therapy with lipiodol injection.

A. S., aged twenty-seven, married seven and one-half years. First seen on May 24, 1930. Patient gave a history of having had an abortion of four months' gestation shortly after marriage with a subsequent sterility. She had a very slow convalescence following the abortion but claims not to have been very ill. With the exception of a history of gall bladder disease with operation of cholecystostomy and appendectomy in February, 1929, complicated by phlebitis of the left leg, her past history was uneventful. No history of any vaginal discharge or any pelvic infection could be obtained.

Examination showed a well-preserved woman, apparently strong physically, height five feet and seven inches, and weight one hundred and thirty-five pounds. There were no obvious marks of endocrine dysfunction. Thyroid was not enlarged. Catamenia normal, twenty-eight day interval, lasting four to five days, moderate in amount.

Pelvic examination revealed a normal, noninflammatory vulva. The cervix pointed backward and downward and was not lacerated. There was no erosion, no discharge, and the cervical reaction was alkaline. The uterine body was normal in size and forward. There was no tenderness in the fornices and no palpable masses. The Wassermann was negative and the sedimentation time was one hour and fifty-five minutes. The blood count was normal. The condom test was positive. The Huhner test revealed cervical insemination. Live spermatozoa were found in the cervix within two hours after coitus.

Two Rubin tests done on the fourth day postmenstrual following two consecutive menstrual periods showed the tubes apparently occluded. Pressure went to two hundred, as registered by the mercury manometer.

On October 12, 1930, the uterus was injected with lipiodol (5 c.c. was used), and the pressure reached two hundred. The six- and twenty-four-hour films substantiated the readings as follows: "Hysterosalpingograms show the left tube apparently patulous with considerable iodized oil having entered the peritoneal cavity. There is a mulberry-like collection of iodized oil at the distal end of the right tube suggesting the presence of a hydro- or pyosalpinx." (Fig. 7.)

Following the November and January periods, Rubin tests were repeated and in each the pressure fell at one hundred and twenty and each test was followed very

promptly by the characteristic "shoulder pain" when the patient was allowed to sit up.

In February, the patient was again seized with attacks of acute cholecystitis and a cholecystectomy was done on February 20, 1931, in the Woman's Medical College Hospital. At that time an exploration of the pelvis was made through the upper abdominal incision but there were no palpatory findings in the pelvis; the tubes were apparently normal. The patient was menstruating at the time of the operation. After coitus on March 13, there were no subsequent periods. On December 10, 1931, an eight-pound girl baby was born.

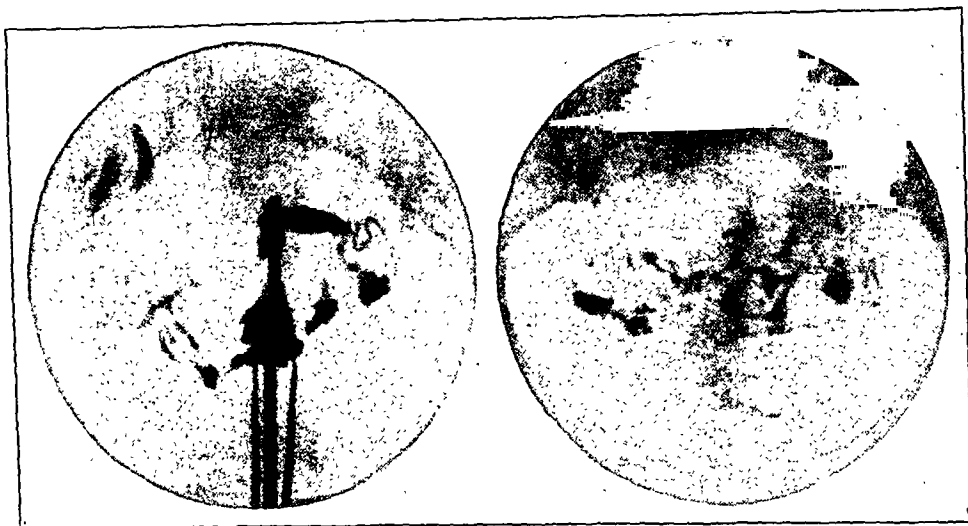


Fig. 7.—Left tube patent. Right hydro- or pyosalpinx.

#### SUMMARY

1. Hysterosalpingography by means of lipiodol is a safe and simple procedure.
2. Hysterosalpingograms made with lipiodol or iodized oil media are of great value in the study of sterility cases and should be considered as a part of the diagnostic armamentarium.
3. In certain cases of sterility the injection of lipiodol is of direct therapeutic value. One case report of a pregnancy following the use of hysterosalpingography in the study of sterility due to occluded tubes was made.

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## GLYCOSURIA IN PREGNANCY

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NOTWITHSTANDING the large amount of work which has been done on the meaning of glycosuria during pregnancy, there is still much uncertainty regarding its significance. Williams,<sup>1</sup> in 500 pregnant women, found glycosuria unaccompanied by clinical symptoms in 13.6 per cent, while Williams and Wills,<sup>2</sup> in 640, found 5.4 per cent with the same condition. Payer,<sup>3</sup> as far back as 1899, found a much higher proportion than this. About one half of his cases showed glycosuria at some time during their pregnancy. Variation is also found in the amount of sugar present in the urine after the administration of sugar by mouth. In these tests 100 grams of glucose are generally given, and glycosuria has been found present in 50 per cent or more of the cases. In fact, it has been suggested that this glycosuria following the administration of glucose might be used as a diagnostic test for pregnancy, especially during the early weeks. The presence of sugar in the urine after a small dose of phlorizin has also been advocated for its diagnostic value. Neither of these, however, has gained universal support. Many observers have noticed that glycosuria has often been present with a normal blood sugar. In other words, that a condition resembling, if not identical with, renal glycosuria was present.

In all of this work it has generally been believed, though the definite observations are not many, that the sugar present during pregnancy, especially in the early months, is glucose, while that present after labor, when the breasts are functioning, is lactose. A few observations of our own have confirmed this.

Glucose and lactose are not alone in having an abnormal metabolism during pregnancy. Gottschalk and Stecker<sup>4</sup> gave 100 grams of levulose and considered the presence of levulosuria as diagnostic of pregnancy, though a negative result was not thought to exclude it. Rowe<sup>5</sup> has shown that the pregnant woman has a lowered tolerance for galactose. She can tolerate only 20 gm. of this sugar without "spilling over" through the kidneys, while the average person can take care of 40 gm. Herold<sup>6</sup> believes that there is, in normal pregnancy, an overfunction of the sympathetic nervous system during the early months, and of the vagus during the later months. He says that these nerves, with their associated glands, act to maintain a normal blood sugar early in the pregnancy and that the blood sugar gradually lowers throughout the succeeding months until about the time of labor, when there is a definite rise and a hyperglycemia occurs. A glycosuria due to a lowered renal threshold may be present during the early months.

Elias, Gudeman, and Roubitschek<sup>7</sup> have found, after intravenous glucose, that, though the blood sugar curve is normal, the threshold is apparently low. Höst<sup>8</sup> says that, during early pregnancy, the glycosuria following sugar intake is due to a high blood sugar, while in the later months the threshold is lowered. Lawrence,<sup>9</sup> from a

small series of cases, concludes that in early pregnancy there is a normal glucose tolerance curve, but a lowered threshold. It is evident from this short review that there is considerable lack of agreement on the occurrence and cause of glycosuria during pregnancy.

The presence of glycosuria may be very irregular. It may occur at any time during pregnancy without being continuous or it may be present all or none of the time. It may be found with one pregnancy and not during a subsequent one, perhaps to return during a third.

It is clear that this sugar must originate either from a high blood sugar concentration which has risen above the normal threshold of the kidneys, as it does in diabetes mellitus, or from a normal blood sugar with a lowered renal threshold.

In the former hypothesis one must assume that pregnancy may be a strain on the sugar metabolizing apparatus of the body. This has not as yet been proved, though it has long been recognized that coincident diabetes and pregnancy accentuate the dangers of both. Some observers have maintained that the pancreatic tissue of the young is a benefit to the mother, especially during the later months, though this has not been confirmed by all other workers. Peckham<sup>10</sup> has found, in a recent series of pregnant diabetic women, that the diabetes was much improved during the later months of pregnancy.

On the other hand, if there is a lowering of the threshold of the kidneys for sugar so that glycosuria is accompanied by a normal blood sugar, the condition would be analogous to renal glycosuria. Observations of this sort have been made from time to time. This condition might result from a direct action of products of pregnancy on the kidneys, or, indirectly, by means of the activities of certain glands, themselves influenced by the pregnant state. It is of great importance that we should know the facts surrounding the origin of this glycosuria more fully. How seriously is glycosuria during pregnancy to be considered, and does pregnancy have any importance in the etiology of diabetes? Joslin<sup>21</sup> has pointed out the harmful influence of diabetes on pregnancy. He further states that subsidence of glycosuria after labor does not remove the possibility of diabetes appearing later.

For the purpose of ascertaining the relative proportion of women who may have sugar from either of these two causes, we have done a sugar tolerance test on 247 women who came to the clinic for prenatal care. The group as a whole are almost consecutive in their first appearance at the clinic. The only exceptions to this are a few women who for one reason or another, refused to submit to the test. The first urine examination was made at the time of the test so that there were no patients included because they did or did not have sugar in the urine. The sugar tolerance test, while still not completely understood, is generally considered to depend largely on the function of the islands of Langerhans of the pancreas for its result. If the function of these islands of the gland is normal, a measured amount of sugar, given by mouth, is taken

care of by body in such a way that, if blood sugar determinations are made before and after the sugar intake, the determinations one-half hour and one hour after the sugar will not be too many points (0.150 per cent to 0.160 per cent) above the fasting specimen (0.080 per cent to 0.120 per cent), and the specimen taken at the end of two hours will have returned to the level of the fasting specimen. During this time no sugar should escape from the blood through the kidneys into the urine. When the function is deficient, the one-half hour blood sugar usually rises to or above the threshold point of approximately 0.180 per cent, the specimens at the end of one hour and two hours will reach as high or higher than the one-half hour specimen, and the return to normal will usually be delayed well beyond the two hours. This, in general, is the type of curve found in diabetes mellitus.

A fasting specimen of blood was procured from each of the patients by venepuncture, and 1.75 gm. of dextrose per kilogram of body weight was given, dissolved in water. Specimens of blood were then collected one-half hour, one hour, and two hours after the sugar intake. The patient voided urine before the sugar was given. A specimen of urine was then collected at the time of taking the last blood sugar and examined qualitatively by Benedict's test, using 8 drops of urine and 5 c.c. of the solution. If it became necessary for the patient to void during the test, all specimens so voided were examined. We have divided the blood sugar curves obtained in these patients into, (1) those in which there is found nothing unusual, (2) those in which there has apparently been a loss of tolerance, and (3) a few which we called doubtful, because, while they were not normal by our criteria, they were certainly not markedly abnormal.

We have taken a blood sugar of 0.140 per cent or over at the end of two hours after the ingestion of sugar by mouth, and of 0.170 per cent or over at any time during the two hours, as evidence of a defective sugar metabolism. As has been mentioned, below 0.180 per cent there should be no gross sugar present in the urine. The normal and abnormal blood sugar curve groups have been further divided by the presence or absence of sugar in the urine specimens in large enough amount to be determined by Benedict's qualitative test. In this way we have six groups of patients as shown in Table I.

TABLE I

	CASES	PER CENT
Normal blood sugar curve and no sugar in urine	150	60
Doubtful blood sugar curve and no sugar in urine	16	6
Abnormal blood sugar curve and no sugar in urine	6	2
Normal blood sugar curve with sugar in urine	49	20
Doubtful blood sugar curve with sugar in urine	11	4
Abnormal blood sugar curve with sugar in urine	15	6
Total	247	

It will be noted in this table that 60 per cent of the patients are normal both as regards the response of their blood to the sugar ingested and as regards the absence of sugar in the urine. These women act as we would expect of normal men and nonpregnant women as regards their response to these tests. There is no apparent condition present which would reduce their normal ability to metabolize the standard amount of sugar in the standard length of time. In addition there is no alteration of the kidneys either normal or abnormal, at the time of the test, which causes these organs to allow the escape of any gross sugar into the urine from a normal blood sugar concentration.

The second largest group, 20 per cent, showed a normal blood sugar curve indicating a normal metabolism of carbohydrate. At the same time, however, they excreted sugar into the urine from a blood sugar definitely below the normal kidney threshold. A certain number of these patients with sugar in the urine had a maximal blood sugar at some time during the two hours of 0.140 per cent to 0.150 per cent. On the other hand, many were not above the upper normal of 0.120 per cent, and many others with blood sugars around 0.150 per cent had no urine sugar. This urine sugar varies from a small amount to several per cent. Any with doubtful sugar tests were not included as positive. There were a total of 8 per cent who had a blood sugar curve on the basis of which a diagnosis of diabetes mellitus or lowered carbohydrate tolerance would usually be made. Of this number 6 per cent had sugar in the urine also, while 2 per cent had no sugar, due probably to a kidney deficiency, which was definitely determined in some of the cases. In all, about 80 per cent of these patients showed a normal pancreatic response, while, of the remaining, about 8 per cent showed a blood sugar curve such as is generally considered to designate a diabetic state or at least a reduced efficiency of the pancreas, and a little over 10 per cent were doubtful. As these patients with doubtful curves showed no clinical symptoms, we are including them with the normal sugar curves for the purpose of study.

TABLE II

MONTHS	NORMAL BLOOD URINE NEGATIVE		ABNORMAL BLOOD URINE NEGATIVE		NORMAL BLOOD SUGAR IN URINE		ABNORMAL BLOOD SUGAR IN URINE	
3½ and below	8	67%	0	—	4	33%	0	—
4 and 4½	14	78%	0	—	4	22%	0	—
5 and 5½	36	63%	2	4%	13	23%	6	11%
6 and 6½	41	63%	4	6%	18	27%	3	5%
7 and 7½	25	69%	0	—	8	23%	3	8%
8 and 8½	13	65%	0	—	7	35%	0	—
Totals	137	68%	6	3%	54	27%	12	6%

The statement has been made from time to time, that there is a difference in sugar excretion between the early and the late months of pregnancy. Our cases do not bear this out in any way. (Table II.) Notwithstanding the small number of cases in each month, when they are divided, we feel that they show a remarkably small variation from the total average; namely, three and one-half to four and one-half and eight to eight and one-half months, are respectively early and late, and we are inclined to think that with a larger number of cases they might have been closer to the average of the total. Statistical analysis shows that the variations of the different months are not significant.

The patients who showed a diabetic type of curve are being followed and a further study of them will be reported later.

There is no appreciable difference between the primiparae and the multiparae, as is shown in Table III.

TABLE III

	NORMAL BLOOD URINE NEGATIVE		ABNORMAL BLOOD URINE NEGATIVE		NORMAL BLOOD SUGAR IN URINE		ABNORMAL BLOOD SUGAR IN URINE	
Primiparae	54	68%	2	3%	21	27%	2	3%
Multiparae	59	67%	1	1%	24	27%	5	6%

In our examinations of urine the presence of sugar was determined by the qualitative Benedict test, using the standard technic. However, as this test does not show small amounts of sugar, it occurred to us to determine whether there was any glucose, however small in amount, in the urines of pregnant women generally.

It is well known that reducing substances are present in the urines of all persons. Folin<sup>12</sup> has stated that these reducing substances are polysaccharide sugars from the food and other bodies, noncarbohydrate in character, which the body is unable to utilize and so excretes by way of the kidneys. He further states that none of this microscopic sugar is glucose. The total amount of these reducing substances varies considerably depending largely upon the diet and, in women after labor, upon the lactose from the functioning breasts. In most normal urines figures for these reducing bodies will be found to lie between 20 and 70 mg. per 100 c.c. of urine. To measure any glucose present the method of fermentation and reduction was used.

This method consists in determining the amount of reduction before and after a short fermentation with yeast. As any glucose present will be fermented out by the yeast, the amount of glucose originally present in the urine will be the difference in the amount of reduction before and after fermentation. The reduction method used was that of Folin and Svedberg.<sup>13</sup> Urine specimens from 50 consecutive women attending the prenatal clinic and from 50 consecutive women on the twelfth day fol-

lowing delivery were examined. In Tables IV and V are shown the results of these examinations.

In the first group of 50 urines from women during pregnancy 45, or 90 per cent, showed the presence of glucose. The amount of glucose found varied from 4 mg. to 132 mg. per 100 c.c. of urine, with an average of 38 mg.  $\pm 4.7$  per 100 c.c. of urine. In other words, the urines of most of the 50 pregnant women contained glucose, which is probably not present in nonpregnant women and in men. In the second group of urines from women twelve days after delivery only 21 out of the 50, or

TABLE IV. FERMENTABLE SUGAR (GLUCOSE) IN URINE DURING PREGNANCY

REDUCTION BEFORE FER- MENTATION	REDUCTION AFTER FER- MENTATION	DIFFERENCE (GLUCOSE)	REDUCTION BEFORE FER- MENTATION	REDUCTION AFTER FER- MENTATION	DIFFERENCE (GLUCOSE)
36 mg.*	23	13	70	54	16
72	21	51	96	54	41
40	27	13	27	19	8
56	40	16	68	25	43
160	96	64	136	125	11
48	40	8	200	142	58
192	134	58	114	102	12
100	28	72	112	90	22
157	47	110	48	30	18
64	ft. tr.	64	84	74	10
68	ft. tr.	68	108	61	47
84	ft. tr.	84	50	40	10
124	65	59	112	52	60
98	64	34	59	53	6
196	97	99	176	44	132
32	21	11	34	30	4
128	30	98	54	42	12
103	63	40	Glucose average 38 mg. $\pm 4.7$		
65	49	16	The following specimens showed no fermentable sugar		
42	24	18	44	46	-
83	43	40	27	29	-
88	48	40	114	120	-
88	51	37	45	45	-
52	32	20	82	77	5
44	29	15	Average of nonfermentable reducing bodies 52 mg. $\pm 4.6$		
88	78	10			
45	32	13			
80	54	26			

\*Milligrams per 100 c.c. of urine.

42 per cent, showed glucose. In this group the amount of glucose varied from 6 mg. to 66 mg. per 100 c.c. of urine, with an average of 26 mg.  $\pm 3.8$  per 100 c.c. of urine. These examinations were made on the twelfth day after delivery because on that day patients are allowed to leave the hospital, thus making it difficult to get further specimens. Apparently by the time the women leave the hospital the cause of the glucose excretion has ceased completely in over one-half, and in the others it has been reduced in its effect.

Another point of interest appears in the table. It will be noted that the total of reducing bodies is greater by far in the postdelivery than in the predelivery cases. An average of 52 mg.  $\pm 4.6$  per 100 c.c. of urine in the former and 99 mg.  $\pm 8.9$  in the latter. Much of this large amount of nonfermentable sugar is probably lactose associated with the functioning breasts.

TABLE V. FERMENTABLE SUGAR (GLUCOSE) IN URINE ON TWELFTH DAY OF PUERPERIUM

REDUCTION BEFORE FER- MENTATION	REDUCTION AFTER FER- MENTATION	DIFFERENCE (GLUCOSE)	REDUCTION BEFORE FER- MENTATION	REDUCTION AFTER FER- MENTATION	DIFFERENCE (GLUCOSE)
58 mg.*	52	6	80	75	5
72	33	39	60	56	4
112	46	66	416	406	10
192	142	50	128	122	6
80	33	47	112	120	-
114	82	32	146	142	4
62	33	29	122	131	-
66	56	10	129	132	-
26	15	11	88	86	2
80	63	17	112	110	2
80	68	12	92	96	-
104	88	16	123	131	-
104	91	13	208	197	13
72	64	8	44	40	4
92	75	17	80	80	0
96	61	35	130	127	3
240	205	35	168	166	2
108	84	24	136	140	-
160	136	24	152	160	-
136	117	19	84	84	0
96	56	40	120	121	-
Glucose average 26 mg. $\pm 3.8$			32	32	0
The following specimens showed no			16	16	0
fermentable sugar			22	22	0
100	98	2	96	100	-
128	127	1	132	121	11
88	88	0	Average of nonfermentable reducing bodies 99 mg. $\pm 8.9$		

\*Milligrams per 100 c.c. of urine.

We would suggest, as a possible cause for the presence of glucose in the urines of pregnant women, that it results from a damage to the tubules of the kidney. It has been pointed out by Van Slyke<sup>14</sup> and by the authors<sup>15</sup> that damaged kidneys may excrete microscopic sugar in a larger amount than normal kidneys. In the kidney of pregnancy there is known to be a certain amount of tubular damage. The presence of glucose in the urine of pregnant women might result from a definite damage to the cells of the tubules.

From these examinations it seems that while most pregnant women showing sugar in the urine are not in any way diabetic, there are a few who show a lowered tolerance for sugar. Whether this condition is limited to the term of the pregnancy, or whether it is permanent, first ap-

pearing during pregnancy, is not as yet clear. Evidence as to whether sugar in the urine of a pregnant woman is due to lowered tolerance with a hyperglycemia or to a condition analogous to renal glycosuria, with a normal blood sugar, can be procured by a sugar tolerance test.

### CONCLUSIONS

1. Sixty per cent of pregnant woman show no gross abnormalities of sugar metabolism.
2. Twenty per cent of pregnant women have gross sugar in the urine following an intake of 1.75 gm. glucose per kilogram body weight, without abnormality of the blood sugar curve.
3. No definite variation is found in the different periods of the pregnancy.
4. No difference is found between primiparae and multiparae in excreting sugar.
5. Ninety per cent of women during pregnancy show microscopic traces of glucose in the urine.
6. On the twelfth day of the puerperium only 42 per cent of women still have glucose in the urine in microscopic quantity.
7. Eight per cent of women during pregnancy show a blood sugar curve on which a diagnosis of lowered carbohydrate tolerance would usually be made.

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Szenes: Lymphogranulomatosis of the Internal Female Genitalia and Bladder. Ztschr. f. Geburtsh. u. Gynäk. 96: 121, 1929.

Lymphogranulomatosis is a chronic inflammatory condition affecting the lymphatic structures, especially the lymph glands. The author reports a case in a thirty-five-year-old woman of a typical lymphogranulomatosis which was verified pathologically. The involvement of the bladder and internal genitalia was very marked and was not amenable to treatment.

DR. LESTER E. FRANKENTHAL, JR.



## PREGNANCY AND DIABETES

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AND

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MRS. B. Mc., aged 34, was referred by Dr. Whitman Rowland, November 21, 1927, for obstetric care. Her father died at sixty-four, her mother from diabetes at sixty-four. One sister living and well. Three brothers died in infancy. The patient had acute rheumatic fever at sixteen years of age, but following the removal of tonsils, recovered. Has never had any other illness and has normally weighed 150 to 160 pounds. Menstruation began at fifteen, irregular, four to five days, no pain, until seven years ago when periods became regular. Since August 3, 1927, she has not menstruated.

Married twelve years, no precaution against pregnancy. Husband fifty years of age. Was well until two years ago when patient first noticed vaginal discharge associated with extreme tenderness and redness of vulva and vagina. The vulva was covered with small white blisters. Itching was intense. She was seen by a physician who treated her for vaginitis, but since she received little benefit, she discontinued treatment. On November 14, 1927, one week before coming to see me, she had consulted Dr. Rowland on account of this intense itching of the vulva. She suspected that she was undergoing a change of life in that she had started skipping periods. She had noticed extreme thirst for some time and she had passed large quantities of urine frequently. Her appetite ravenous, but in spite of this there had been a gradual loss of weight, and she had a constant weakness with pains throughout both legs for some time.

Examination revealed a markedly dry, glassy, excoriated vulva and vagina, and a uterus enlarged about the size of a three and one-half to a four months' pregnancy. Examination of the urine revealed a marked sugar reduction and tentatively with the history and the physical findings and the sugar in the urine, a diagnosis of diabetes mellitus and pregnancy was made. On a fasting stomach a blood sugar of 205 mg. was found. A quantitative estimation of sugar in the urine revealed 7.14 per cent sugar in 2100 c.c. of urine. Fermentation test was positive with 0.25 mg. to the 10 c.c. of urine. She was placed on a 1407 calorie diet and 15 units of insulin daily and was referred to me for confirmation of the diagnosis of pregnancy.

On February 26, 1927 the diagnosis of pregnancy was confirmed. Blood pressure 115/60. Urine negative except for 4-plus sugar. Weight 131 pounds. She improved on the diet and insulin. As it is often difficult to estimate the exact diet necessary for a pregnant woman with diabetes her diet was increased to 1800 calories, but continued with the same amount of insulin. Even with this the patient complained of extreme hunger and her diet was increased during the latter part of the fifth month to 2345 calories with insulin 20 units. Her blood sugar had dropped from 205 mg., during the fourth month to 147, and during the first part of the fifth month it dropped to 140; during the latter part of the fifth month it took a jump to 200 mg. Presuming that this diet was too heavy it was again reduced to 1800 calories, which was continued throughout pregnancy with 15 units of insulin. During the sixth month her weight increased to 143 pounds and the blood sugar had fallen to 180 mg. During the seventh month her weight had jumped to 146 pounds. Blood sugar dropped to 170 mg. Urine remained negative for sugar, acetone, and

diacetic acid throughout the remaining gestation. During the eighth month the blood sugar continued to drop and her weight dropped to 143 pounds. She was feeling extremely well and during the ninth month her weight went to 150 pounds, although the blood sugar had returned to 85 mg. The blood pressure had jumped, however, to 142/90. Urine was negative for albumin.

On May 21, 1928 she was admitted to the Methodist Hospital with the onset of labor. Blood pressure 165/90, 8 A.M. blood sugar 143 mg., urine negative. She was given a comparatively full carbohydrate diet so that she might be prepared for labor or operation. 8 P.M. blood sugar 85 mg. Urine negative for acetone and diacetic acid and at 9:30 P.M. a cesarean section was performed under a local anesthesia. Upon opening the uterus virtually no amniotic fluid was found and a living male child (5 pounds 2 ounces) was delivered. Uterus was closed in the usual manner and a modified Irving's method of tubal sterilization was carried out. She was returned to her room in excellent condition.

For the first twenty-four hours postpartum, there was a fall in the morning blood sugar to 107 mg. followed by a slight elevation of the evening's to 112 mg. associated with a rise in blood pressure to 177/90. The urine remained negative. Orange juice and fluids were given by mouth for the next forty-eight hours. An elevation was noted in the blood sugar to 120 mg. at 8 A.M. with a further increase in the evening's to 122 mg. The urine remained negative with the blood pressure dropping to 167/90. On the third day there was evidence of a mild acidosis, as shown by the presence of acetone and diacetic acid and a one-plus sugar in the urine. This day the morning blood sugar registered 112 mg. while the evening's had increased to 127 mg. The patient was given a small amount of soda solution by rectum. On the fourth day because of the acidosis, as previously mentioned and the continued rise of blood sugar at 8 A.M. to 135 mg. and at 8 P.M. to 140 mg., five units of insulin were added, plus a carbohydrate diet. Even with the additional dosage of insulin, the blood sugar continued to rise on the fifth day to 190 mg. in the morning, with a slight diminution in the evening to 152 mg. The urine showed a three-plus reduction for sugar, however, the acetone and diacetic acid had cleared up. Therefore, the insulin was increased on the sixth day to ten units with a moderate reduction in the morning blood sugar, but a decided increase in the evening. This additional dosage of insulin later, however, resulted in a continued lowering until 115 mg. was reached on the ninth day. Because of economic conditions the mother was discharged home in an ambulance on the ninth day, having fully recovered from the operation with primary union of the abdominal wound. For the next thirty days the patient was comparatively well, but following this, she began to have pains in the region of her right sciatic nerve. She was in excellent condition from a diabetic standpoint, but it was assumed that this was probably a mild diabetic neuritis. A search was made for all possible foci of infection and these were removed, but all efforts failed to relieve this excruciating agony which required morphine at regular intervals. The sciatica persisted for many months, finally becoming ameliorated either coincidental with or following the use of arsenic intramuscularly. To date she still remains upon a very rigid diabetic diet and is taking moderate doses of insulin, but is in very poor health. Her baby was placed on a modified milk formula and continues to thrive and shows no evidence of diabetes.

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# FETAL MORTALITY AS AFFECTED BY THE DURATION OF LABOR\*

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IN A recent communication the author presented the results of a study of a large series of consecutive deliveries at the Johns Hopkins Hospital in which the effect of race and age of the patient on the duration of labor was calculated. It was shown that colored women, of all age groups, had a longer mean duration of labor than the white. Since it is also known that the fetal mortality is higher in the black than in the white race, it seemed advisable to investigate to what extent this mortality is influenced by the duration of labor, with particular reference to any existing racial disparity.

For this purpose the above mentioned series of cases was employed, namely 13,658 women consecutively delivered at term at the Johns Hopkins Hospital and divided according to race and parity as is shown by the accompanying figures.

	WHITE	BLACK	TOTAL
Primiparae	3742	3880	7622
Multiparae	3352	2684	6036
Total	7094	6564	13,658

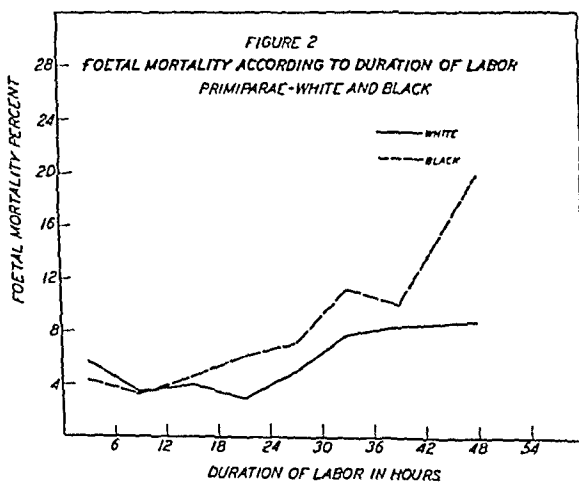
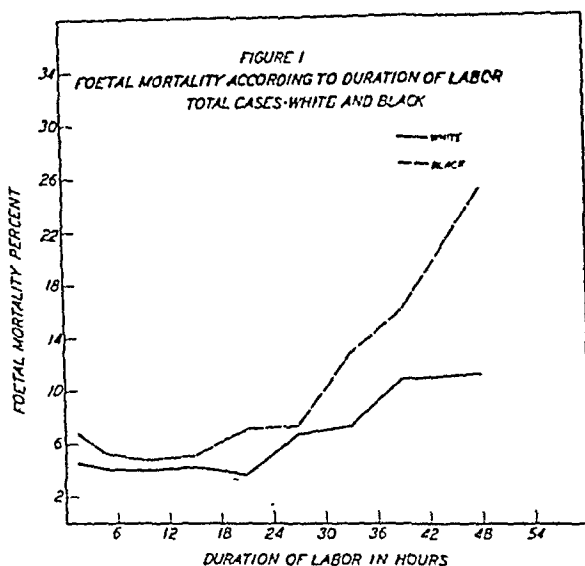
This group of cases does not include any prematurely delivered women, likewise all instances of cesarean section are omitted, together with some few cases in which the hospital records are lacking in definite information as regards total duration of labor.

Fig. 1 shows the fetal mortality as influenced by length of labor for the total cases in the series, including primiparae and multiparae, and spontaneous and operative deliveries. It will be noted that the mortality in the whites is higher in the precipitate labors (under three hours) than during the optimum period of three to twenty-three hours. In labors of eighteen to twenty-three hours the lowest mortality rate is observed (3.73 per cent), and from this point a rapid and steady rise occurs so that a mortality of 11.33 per cent is observed in those labors whose duration is forty-two hours or more. A similar trend is observed among the blacks, although here the optimum figure of 4.74 per cent is observed in those labors of duration six to eleven hours, with a rise thereafter, which in labors of forty-two or more hours reaches 25.18 per cent. In other words, a rise in mortality rate among the blacks is observed in labors twelve hours shorter than in the whites, and the rate of increase is much more rapid.

Regardless of duration of labor, the black fetal mortality rate is higher than that observed in the whites, and the difference becomes more

\*In the printing of this article, a series of tables giving in detail the statistical data on which this article is based has been omitted owing to lack of space.

marked as the duration of labor increases, so that when it lasts forty-two hours or more, the fetal mortality is 13.85 per cent higher in the black women. In both races there occurs a much higher mortality with prolonged labor, but it seems obvious that the black infant stands a prolonged labor proportionately worse than the white, as is evidenced by the fact that the mortality rate in white infants is 3.04 times as great when the labor lasts over forty-one hours as during the optimum period,

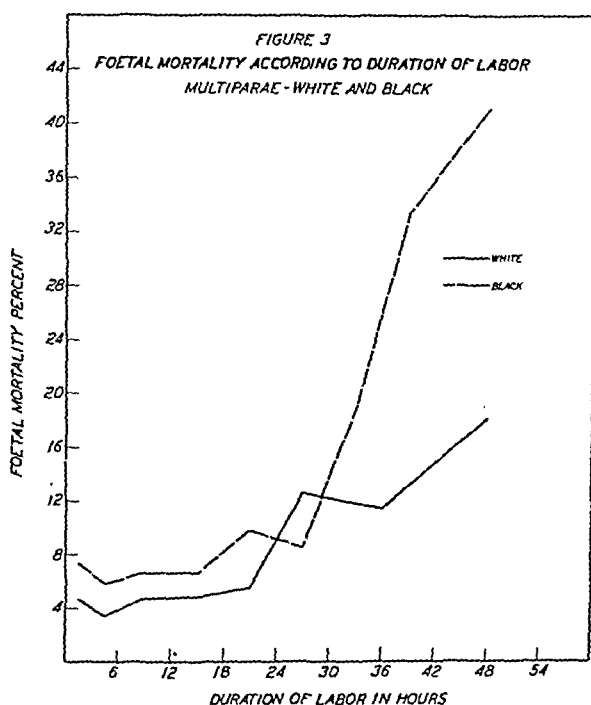


whereas in black infants the mortality, considered from a similar point of view, is 5.31 times as high.

Fig. 2 shows the effect of duration of labor on fetal mortality in primiparae of the two races. Just as when all types of patients were considered, there is a relatively increased rate in precipitate labors, an optimum in labors of normal length, and a very high mortality when the course of parturition is prolonged. Also, a rising mortality is observed twelve hours earlier in the black than in the white women, and

in the prolonged labors the black infant mortality becomes disproportionately high. Indeed, in black patients with labors of forty-two or more hours the mortality is 19.51 per cent, a figure 6.15 times as high as the optimum rate in labors of six to eleven hours, whereas in the whites the lowest mortality is that of 2.91 per cent in labors of eighteen to twenty-three hours, which is increased only 3.01 times in the forty-two hour or more group; or, in other words, the black infant stands prolonged labor only half as well as does the white.

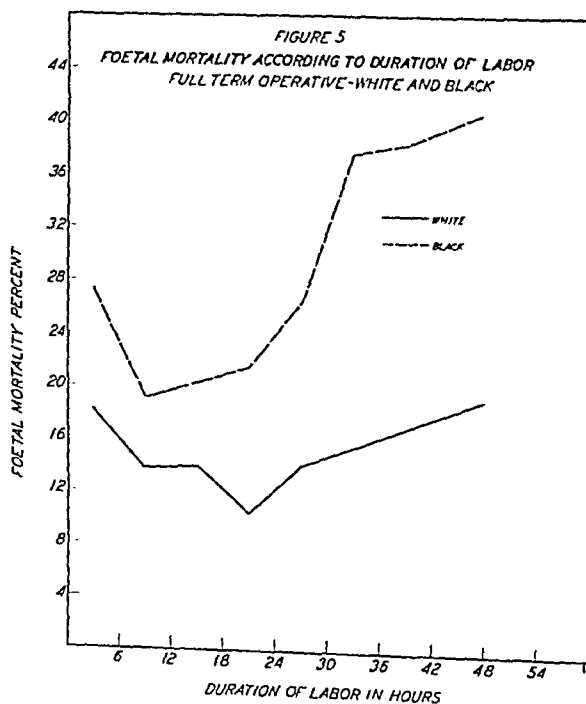
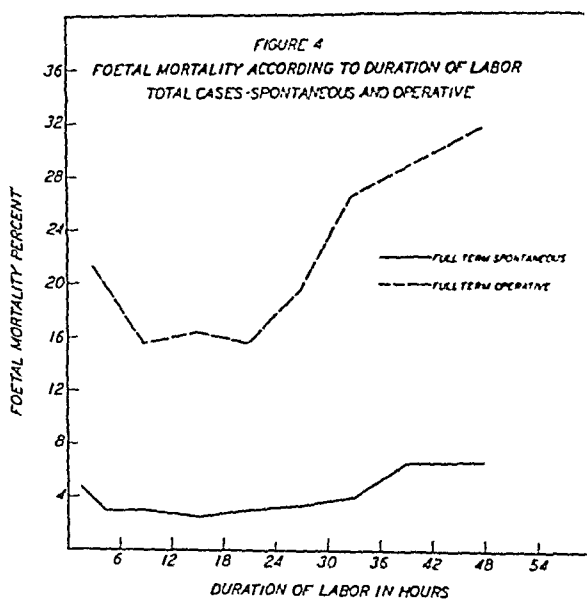
Fig. 3 presents the case for the multiparae of the two races. In general the statements made concerning the total cases and primiparae obtain here, except that the optimum mortality rate for both races occurs in the three to five hour duration group and rises from that time.



The  $\frac{\text{Prolonged}}{\text{Optimum}}$  labor ratio among multiparae is 6.96 in the black as contrasted with 5.32 observed in the white race.

The fetal mortality in operative labors is extremely high in this clinic (19.71 per cent). This is due to a considerable extent to the large number of neglected cases admitted. Although these emergency cases are divided approximately equally between the two races, yet the fetal mortality is almost twice as high in the blacks as the whites, being 27.01 per cent and 14.58 per cent, respectively. Fig. 4 offers a comparison between the results of operative and spontaneous deliveries, the figures given being a combination of the two races. With both types of delivery the mortality is higher in precipitate labors than in those of normal dura-

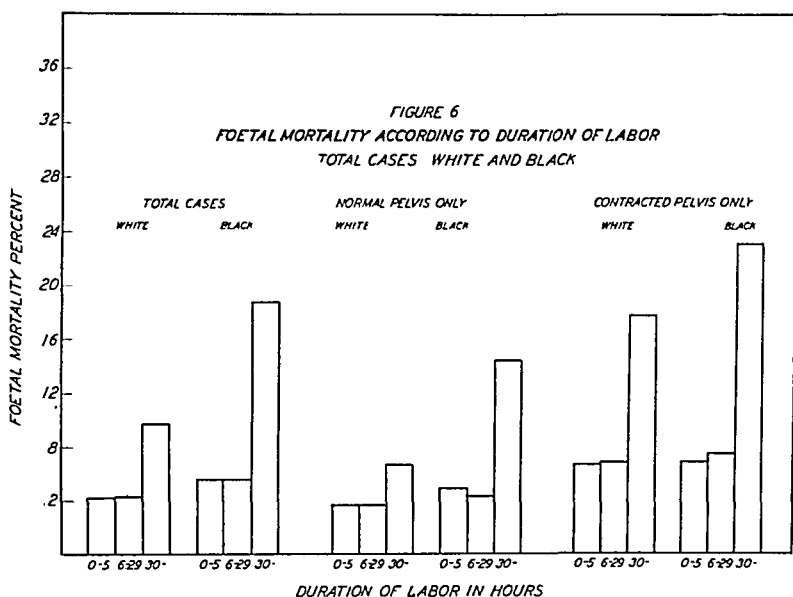
tion. With prolonged labor the rate again rises, but more sharply when the labor is terminated by operative means. Thus, the difference in mortality percentage between prolonged and optimum labor is 4.18 per cent among spontaneous deliveries, as contrasted with 16.10 per cent



in the operative types. Accordingly, it seems evident that when the labor has continued for thirty or more hours the fetus tolerates operative delivery from below very poorly, regardless of the method used. It has frequently been our experience that a simple low forceps delivery,

undertaken to terminate a prolonged labor, results in a dead-born child, although the fetal heart had been in good order shortly before operation. The explanation of this phenomenon is not evident, although it may to some extent be due to the fact that in such cases the child seems to tolerate very poorly the administration of a general anesthetic to the mother.

Fig. 5 offers a comparison between the results in operatively delivered cases among the two races. It will be again observed that the optimum results in the colored race occurs with labors twelve hours shorter than is the case among the whites. In other words, the mortality rate begins to increase in labors of twelve hours or over in black women, whereas such an increase is not noted in the whites until the twenty-four hour duration is attained. The black women delivered by operative means



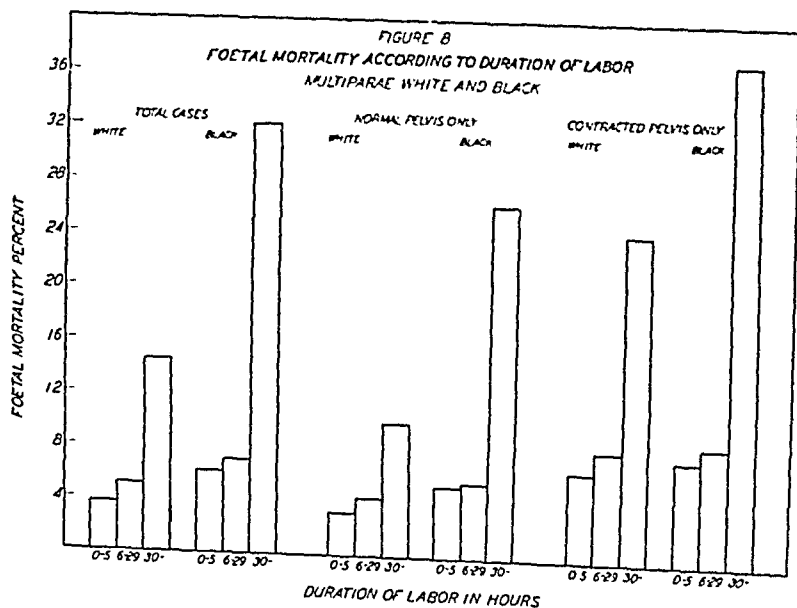
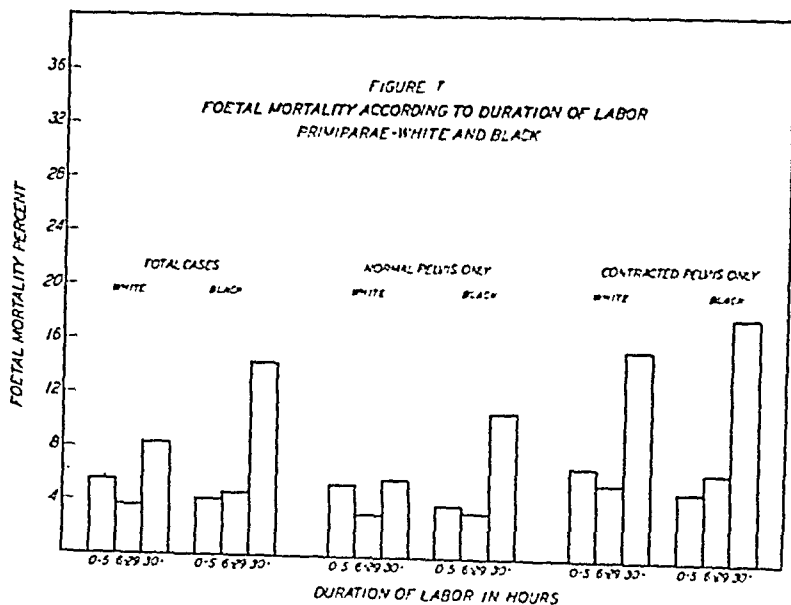
after a prolonged labor show an extremely high fetal mortality as contrasted with the white, and the  $\frac{\text{Prolonged}}{\text{Optimum}}$  labor duration ratio is 2.08 and 1.85 in the two races, respectively.

Figs. 6 to 10, inclusive, illustrate the before mentioned age and racial differences, with added information concerning pelvic contraction. We have arbitrarily divided the duration of labor into three time groups, and assume a labor under six hours to be precipitate, one of thirty or more hours to be prolonged, and with the intermediate duration normal.

A study of Fig. 6 indicates that for both races there is very little difference in mortality between the short labors and those of normal duration. With prolonged labor, however, the mortality rate becomes greatly increased, and more so in the black than white women, as is evidenced by calculating  $\frac{\text{Prolonged}}{\text{Normal}}$  labor duration ratios. Thus, when we con-

sider the total cases in the series, those with normal pelvis, and those with contracted pelvis, we obtain the following set of ratios:

	WHITE	BLACK
Total Cases	2.25	3.32
Normal Pelvis	1.82	3.34
Contracted Pelvis	2.61	3.09

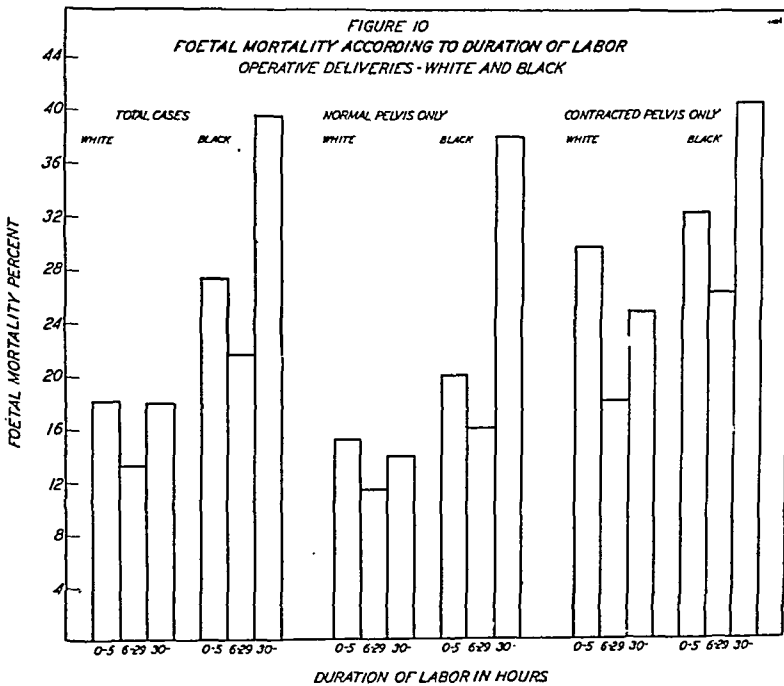
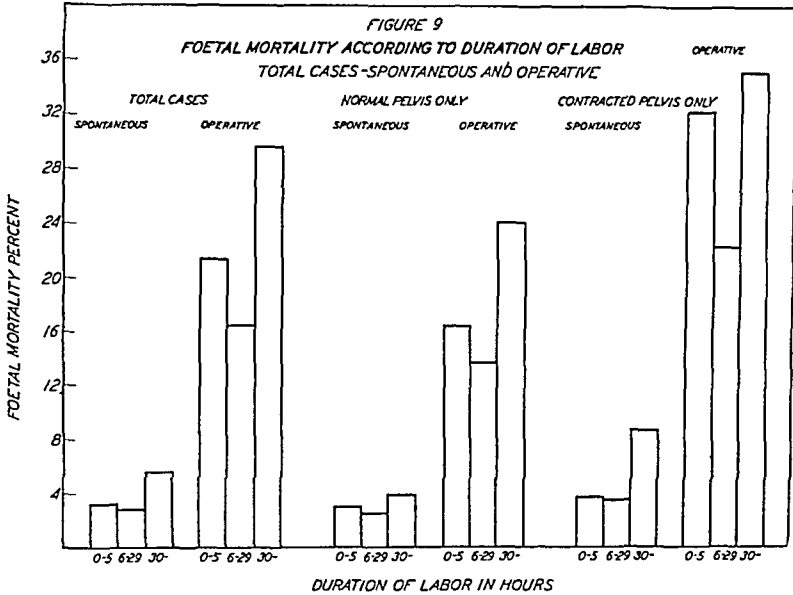


These figures indicate not only the racial difference but also show that in the white race the poor results obtained after prolonged labor are to a considerable extent due to contracted pelvis, as is evidenced by ratios of 1.82 and 2.61 for normal and contracted pelvis, respectively. Attention is also drawn to the extremely high mortality rate in the contracted pelvis cases after prolonged labor, as percentage mortality rates



of 17.73 and 22.87 per cent are found among the whites and blacks, respectively.

Fig. 7 indicates the mortality according to duration of labor and pelvis for the primiparae in the series, while Fig. 8 indicates the same for the multiparae. No comment on these figures is necessary, except to again



direct attention to the high mortality found in prolonged labor with contracted pelvis in the two charts. It will also be observed that with prolonged labor among multiparae there is an even worse prognosis for the child than is the case in such labors with the primiparous woman.

A further comparison between the effects of operative delivery on the child is offered in Fig. 9, which again shows that with normal pelvis prolonged labors are not particularly dangerous if the termination is spontaneous. Operative delivery throughout is attendant with high fetal mortality, and in contracted pelvis with prolonged labor over a third of the infants succumb. Indeed, a mortality of 26.45 per cent is found in cases of this type when all labors are included, regardless of duration.

Finally, the poor results of operative delivery occurring in white and black women are depicted in Fig. 10, and again illustrate the fact that the black infant tolerates this type of delivery much more poorly than the white. However, as has been said, the high rates observed here are due in great part to the large numbers of neglected emergency cases. It would, however, seem that far too many babies are lost as the direct result of operation, and we shall discuss this feature later on.

#### DISCUSSION

An analysis of the effect of duration of labor on fetal mortality in a series of 13,658 consecutive deliveries reveals a marked correlation between prolonged labor and high fetal death rate, as well as significant differences between the white and black races. In both a precipitate labor (under three hours) is not favorable to the baby. Such a labor is usually accompanied by extremely frequent and forceful uterine contractions which by driving the fetus rapidly through the birth canal tend to produce a high incidence of deep asphyxia or intracranial hemorrhage. As would be expected, the unfavorable result of precipitate delivery is observed to a greater extent in the primiparous than in the multiparous woman, since in the latter both the cervix and vaginal tissues yield more readily and the fetus is subjected to less pressure and trauma.

In the white woman, both primipara and multipara, very little difference is observed in fetal mortality with labors of over three and under twenty-five hours' duration. However, when the labor continues for more than the last mentioned period, it is accompanied by an increased mortality rate which for the total whites reaches approximately 11 per cent after the thirty-six hour period is reached. A consideration of the black women in the series, however, reveals that in them the fetal mortality begins to rise when the labor has lasted more than twelve hours, which is twelve hours sooner than the corresponding rise occurring in the whites. Likewise, with prolonged labor, the fetal mortality rises much more rapidly than is seen in the white race.

Regardless of the duration of labor, a higher mortality rate obtains among the blacks, both primiparae and multiparae. In labors of normal duration this racial difference is not marked, but it becomes highly significant when parturition is prolonged, and when the duration is over forty-two hours, racial differences of 10.73 and 22.92 per cent are observed in the primiparae and multiparae, respectively.

In both races the fetal mortality is naturally much higher among the operatively than the spontaneously delivered cases, since many of the former are either distinctly abnormal or represent emergency admissions after faulty treatment on the outside. However, it seems significant that the rise in fetal mortality with prolonged labor is much greater among the operative cases than in those terminating spontaneously. Repeated instances are at hand of a simple forceps after prolonged labor terminating fatally for the child, and it is our belief that the complete anesthesia necessary for such a procedure is tolerated poorly by the infant. The adverse results of operative delivery and particularly after long labor are much more marked in the black race, in whom there occurs a mortality of over 40 per cent in labors lasting forty-two or more hours.

The tendency toward ever increased conservatism in the treatment of labor complicated by moderate pelvic contraction is undoubtedly one of the great advantages of modern obstetrics, and one which if properly pursued will definitely lower the maternal mortality rate. Our figures show, however, that such a policy is accompanied with an increased risk to the child, as for both races, all durations of labor, and all types of delivery from below, the fetal mortality rates are definitely higher with contracted than with normal pelvis. With normal pelves gross death rates of 3.93 and 5.28 per cent obtain in the white and black races respectively, as contrasted with percentages of 7.92 and 9.17 when some degree of pelvic contraction obtains. If, however, the labor becomes prolonged (thirty hours or over) in a patient whose pelvis is below normal in size, the fetal mortality rises remarkably, and for this series becomes 17.73 and 22.87 per cent for the whites and blacks. Finally, if in such a patient after a prolonged labor an operative delivery is necessary, the fetal mortality is appalling and reaches 24.68 and 40.52 in the two races. A discussion of these results and suggestions for their amelioration are not the province of a statistical paper. We wish merely to point out the increased risk to the child when some degree of pelvic contraction obtains, and particularly when this abnormality is combined with prolonged labor, or instrumental delivery.

#### CONCLUSIONS

1. An analysis has been made of the effect of duration of labor on fetal mortality on a series of 13,658 consecutive deliveries at or near term.

2. In both whites and blacks a precipitate labor (under three hours) is associated with an increased risk to the child.

3. After the above period, very little change is noted in fetal mortality in the white race until the twenty-four hour duration is reached, after which it rises proportionately to the increase in length of labor. A similar rise is noticed among the blacks but begins when the duration exceeds twelve hours.

4. The fetal mortality rate is higher in the black than in the white race, regardless of duration of labor, and the black infant tolerates prolonged labor correspondingly less well.

5. Operative delivery is accompanied by a higher fetal mortality and when such delivery follows prolonged labor the mortality curve rises still more abruptly than if spontaneous termination occurs. Likewise, operative delivery is tolerated by the black infant correspondingly less well than the white.

6. The fetal mortality rate is much higher when labor is complicated by contracted pelvis. In such cases the fetus tolerates operative delivery and prolonged labor poorly. A combination of these three factors results in fetal mortality rates of 24.68 and 40.52 per cent in the white and black races, respectively.

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## THE TREATMENT OF PELVIC INFLAMMATION BY MEDICAL AND SURGICAL HEAT\*

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MUCH has been written on the subject of heat therapy in female pelvic infections. Many former impressions have been modified and some new impressions tabulated as facts are influenced by subsequent observations. The reasons for these seeming contradictions are many and for the most part the very nature of the pathology is responsible for the confusion. The work of Corbus and Chapman, Cumberbach, Gellhorn, Cherry, and others, has advanced the study of medical diathermy. Holden has pointed out the advisability of heat therapy in infections by his use of the Elliott machine, which distends the vagina as well as heats it.

Curtis, Cherry, and Hyams have taken up the use of surgical diathermy in treating lesions of the cervix, and further reference to their work will be made in this paper under a discussion of modes of treatment. The scope of this presentation is to review our work in the application of medical heat and surgical diathermy, and to present the clinical results obtained. In the *Journal of the Missouri State Medical Association*, we reported on the application of medical diathermy in chronic pelvic inflammation. In the July, 1931, issue of the *AMERICAN JOURNAL OF OBSTETRICS AND GYNECOLOGY*, one of us (Roblee) attempted to show the difference between the cautery and electrocoagulation procedures in the treatment of chronic cervicitis, and to classify cervical lesions with reference to treatment.

In October, 1931, at the American Congress of Physical Therapy, we

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\*Read before the St. Louis Gynecological Society, December 11, 1931.

attempted to present the work in medical and surgical diathermy from a physical therapy standpoint.

The outstanding feature of the work emphasizes the futility of believing that any type of heat therapy will improve any and every type of adnexitis. In the virgin with pelvic inflammation, a tuberculous salpingitis or an endometriosis is always to be considered a possibility, while in the matron these conditions are quite rare as compared with other types of pelvic pathology. The more cases of pelvic inflammatory conditions observed and treated by us in our clinical study, the more were we impressed with the tendency toward remission. We believe that simple gonococcic salpingitis, which is subacute or chronic, responds well to selected heat treatments. We must remember, when mixed infection is excluded, that pure gonococcus infection often limits itself, even when no treatment except rest is instituted. When dealing with the clinic type of patient, which comprised most of our series, adequate histories were often unobtainable, and the likelihood of reinfection with the gonococcus was a factor that had to be borne in mind.

We would like to emphasize the difficulty in determining in any case of acute gonorrhea whether the particular infection is truly the first infection or a reinfection, or a flare-up of the original infection, as we believe the history is not wholly reliable in these cases. The reason for mentioning this point is that in our opinion whenever cases of acute gonorrhea improved and were not made worse by active local treatment, they were probably reinfections and not actually acute primary infections.

We feel that a suitable vaginal electrode for medical diathermy should possess the following characteristics: first, that it should be distensible and of sufficient size to occupy a large portion of the vaginal vault, adnexal, and culdesac regions; second, it should have contact with the cervix uteri; third, it should be completely insulated from the vulvo-vaginal junction. When a technic with such an electrode was carried out, we were able to diffuse heat throughout the pelvis to such an extent that thermometers placed within the cervical canal, urethra, and rectum, would record 110° F. during treatment. These were actual tissue temperatures. We feel that heat in excess of this amount is contraindicated, as the threshold of living cell tolerance to heat is only slightly in excess of 112° F. Many observers state that 114° F. is the actual temperature lethal to cell life. Heating the pelvis to this extent causes a hyperemia locally and increases the flow of blood through the pelvis, as witnessed by a drop of from three to four degrees in the pelvic thermometers at a time when the general body temperature is elevated by from one to two degrees, as determined by a thermometer placed under the tongue of the patient. The fall of localized temperature readings to synchronize with the increased general body temperature readings demonstrates the body reaction to prevent the overheating of any localized area. This un-

doubtedly is of central nervous system origin and the vasodilatation follows attempts to disperse the local heat. The pulse rate increases and the patient usually breaks into a profuse perspiration.

Again, let us state clearly that we do not believe it is possible to kill the gonococcus in living tissue by means of these temperatures per se, or any heat temperature compatible with cell life. We do not believe that surgical diathermy is ever permissible in the presence of acute infections, because of the severe local trauma that it produces within the tissue. Our only purpose then in producing pelvic temperatures, is a hope that through the stimulation of a hyperemia certain physiologic changes will combat the existing pathologic condition.

The incidence of chronic cervicitis should be sufficient stimulus for the study of its treatment, but when to this is added the opinion of such competent observers as Graves, Pemberton, Smith, Davis, Bailey, Novak and Bloodgood, that cervicitis with its subsequent structural changes is a precursor of cancer of the cervix, and that effective treatment of cervicitis actually prevents the development of carcinoma in this region, every effort to treat this condition effectively must be made.

Ninety-five per cent of cancers of the cervix develop in parous women, and in the remaining 5 per cent a history of chronic cervicitis or instrumentation is usually obtainable. Cervicitis in the nulliparous woman without the presence of lacerations, may make epithelial changes of a precancerous nature. So-called erosion is not an ulceration, but a proliferation of columnar epithelium. The cylindrical epithelium is extruded from the narrow cervical canal and under the stimulus of an infection and by the irritation of its new environment, it replaces the normal stratified epithelium of the vaginal portion of the cervix. There is at once set up a constant war of displacement of the squamous epithelial cells by the columnar cells, and vice versa. As a result, the racemose glands of the cervix become blocked by this new cell growth, drainage is stopped, and nabothian cysts are thus formed. The infected material of these cysts produces inflammatory changes in the stromal tissue. The size of the nabothian cysts and the resultant hyperplasia of the connective tissue produce cervixes of two to three times normal size. Ectropion and polypoid formations may take place.

Even physiologically normal childbirth is a severe trauma to the cervix. Eversions and lacerations of a unilateral or bilateral nature frequently result, thus the columnar epithelium which lines the cervical canal is exposed to the trauma of an acid vaginal reaction. The placing of this delicate epithelial tissue in a hostile environment causes rapid cell growth of a glandular formation and infection results because of lack of resistance on the part of this tissue in its new environment. Scar tissue formation resulting from infection may include bits of epithelium, which, according to C. Jeff Miller, are perhaps prone to become malignant at the menopause. All of the above mentioned inflam-

matory changes seen in cervicitis of the nullipara appear to be accentuated by the structural changes caused by lacerations and ectropion in the parous cervix, and polypoid formation rapidly occurs.

We desire to present in this paper a detailed clinical analysis of 100 cases that received medical heat treatments for subsiding, subacute, and chronic adnexitis and cellulitis, including 40 cases of coincident cervicitis treated by surgical heat (electrocoagulation or cautery).

Sixty-five cases received medical diathermy, 35 cases received Elliott treatments in addition to diathermy, 40 of the 100 cases received surgical

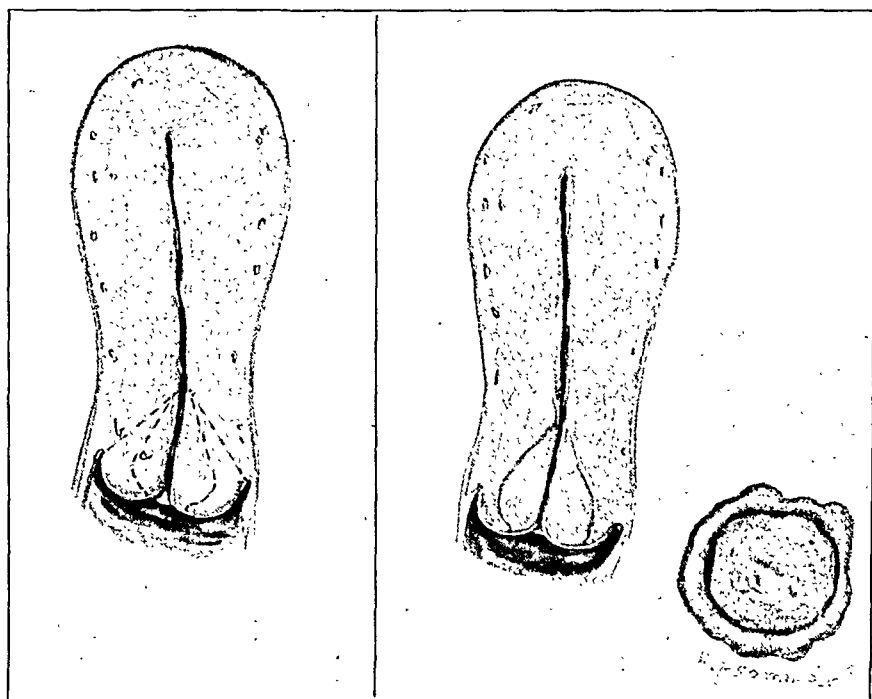


Fig. 1.

Fig. 2.

Fig. 1.—Showing area (a) for subtotal removal of cervix; (b) for complete amputation of cervix uteri by the coagulation method.

Fig. 2.—White area denotes coagulum which will separate in from ten to fourteen days.

heat treatment to the cervix for chronic cervicitis; 36 of these had electrocoagulation and 4 had cauterization.

Of the total number of cases studied, 25 were under active treatment for ninety days, 25 were under active treatment for sixty days, 45 were under active treatment for thirty days, and 5 were under active treatment for fifteen days.

The average age incidence of these patients was twenty-six years. The average total number of medical heat treatments was 18 per patient. Thirty-five patients had Elliott treatments, averaging 10 treatments per patient. Thirty-six of the 100 patients had electrocoagulation of the cervix for cervicitis, and 4 had cauterization. Of the 100 patients

studied in this series 64 had borne children, 15 had had abortions, and 21 had never been pregnant.

The average duration of symptoms before treatment was approximately two years. Ninety per cent of the cases studied had a marked adnexitis; that is, definitely palpable tubo-ovarian mass, unilateral or bilateral, which seemed responsible for the pelvic symptoms. Fifty-six per cent had an associated cellulitis. Fifty-two per cent had marked cervicitis.

Of all patients studied, 73 per cent improved, subjectively and ob-

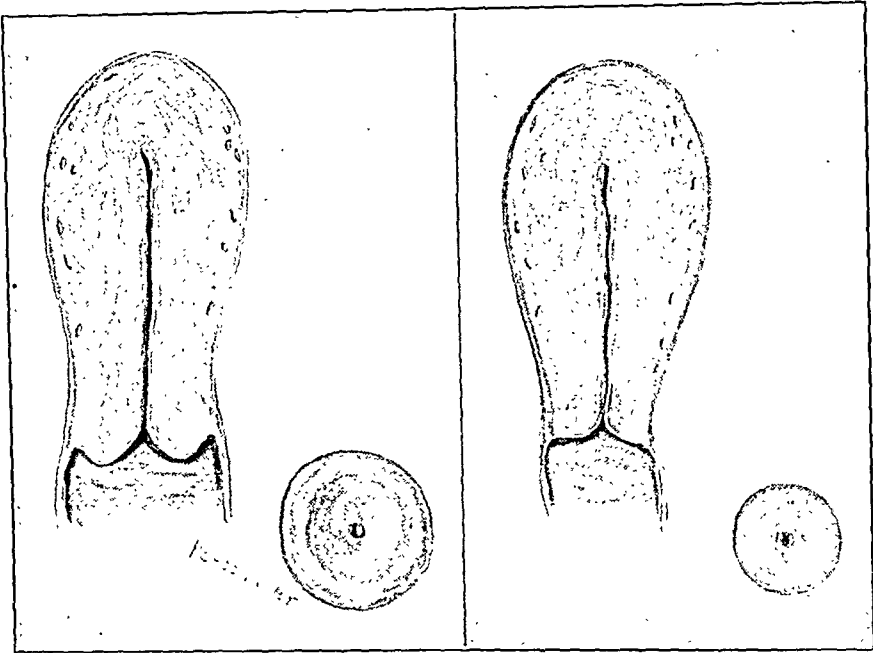


Fig. 3.

Fig. 4.

Fig. 3.—Shows coagulated area clean, with islands of squamous epithelium rapidly covering the clean granulating coned-out area (two to three weeks).

Fig. 4.—Healing with complete squamous epithelial covering as the vaginal pavement epithelium grows over and into the amputated cervical area (five to six weeks).

jectively, while they were being treated. Twelve per cent became definitely worse while under medical heat treatments. Of those who improved while being treated, 50 per cent continued the improvement from two to six months after treatment was stopped. By improvement is meant the patients subjectively felt well, objectively the pelvic masses had disappeared or were smaller, and there was average mobility and lessened or absent cellulitis.

Of the 50 definitely improved patients, 80 per cent had received in addition to the medical heat, surgical electrocoagulation or cauterization of the cervix. Seventy-two per cent had received cervical coagulation, and 8 per cent cauterization. Twelve per cent of the remaining patients treated by medical heat returned to their original condition from two to six months after treatment was stopped. This leaves 36 per cent of



the patients treated by medical heat alone who were somewhat improved over their original condition, yet had subjective and objective pelvic pathology. There remained 2 per cent of the cases that did not remain definitely improved, yet had a cauterization of the cervix in addition to medical heat. There was no incidence of coagulation of the cervix, plus medical heat, that did not remain clinically improved for a period of six months in this series of 36 cases.

We believe that this establishes strong clinical evidence that a chronic cervicitis acts as a focus of infection to the pelvis as a whole. In our larger series of cervicitis cases only, there were 3 patients who had scleratoma and iritis who improved, losing all of their eye symptoms after cauterization and coagulation. These observations led us to attempt to recover bacterial growths from the nabothian cysts of the cervix. The cervix was first cleansed and then seared with a hot instrument, the cyst opened with a sharp knife and the contents taken for a smear and cultures. In cultures so taken from 6 patients there were two growths, one of mixed streptococcus and bacillus infection; one smear and culture was apparently an aerobic streptococcus. Before any conclusions can be drawn a larger series of cases and controlled bacterial studies must be made, with due allowance for possible contamination.

There is quite frequently observed in a routine biopsy an extensive round cell infiltration and the presence of bacteria. We also noted that no case of chronic cellulitis which improved under our medical heat treatments, continued to stay improved so long as the patient had a chronic cervicitis. These patients all improved after coagulation. We had 25 or more cases of marked chronic subinvolution of the uterus, with an accompanying hypertrophy and chronic cystic cervicitis, in which, after coagulation procedures of the cervix were undertaken, the uterus became well involuted within a month's to six weeks' time after the cervix had healed. It is a frequent occurrence in our cases with chronically retrodisplaced uteri, that are more or less fixed, to observe them become freely movable and assume forward, anteflexed positions without additional treatments other than cervical removal by the coagulation method.

In a patient who has passed the childbearing period and the cervix is quite long, cystic, with eversion and erosion and papillary changes, it is the custom now to remove completely this cervix by the same coagulation method carried to a greater extent. The incidence of hemorrhage following such removal is somewhat greater than the subtotal removal that is analogous to the Sturmdorf operation, but if the patient remains off her feet for a week or ten days after such an operation, there are no untoward symptoms. Four cases out of 125 required packing because of vaginal bleeding. This was 3.2 per cent. This percentage does not seem large when one considers that the bulk of the cases were handled as ambulatory in the clinic and did not follow instructions after getting

home. There was no incidence of stenosis sufficient to require dilatation, nor marked symptoms when the proper technic was carried out. However, when coagulation was carried on between two poles of similar size, such intense heat was generated that two of such patients developed stenosis that required dilatation.

At the present time we have on record only two pregnancies following this coagulation procedure, and both have been delivered spontaneously without dystocia or cervical laceration. These patients had a complete removal of the cervix by the coagulation method. Three patients after subtotal removal of the cervix, had diagnostic dilatation and curettage because of irregular uterine bleeding. These three cervixes dilated easily without tearing and clinically showed no evidence of stenosis or excessive scar tissue formation. The curettings showed benign endometrial hyperplasia in two cases, and a senile endometrium in the third.

It would not be physically possible to remove the cervix as completely by the cautery as by coagulation. In addition to this the cautery knife itself is hot and imparts its heat to the cervix by contact. The outside of the cervix is first burned to the point of carbonization and any heat penetration is retarded by the insulating effect of such charring. Carbonization takes place with the cautery because the cautery and the tissue being cauterized are exposed to the air. Clinically, we have demonstrated that carbonization subsequently produces scar tissue. On the other hand, the coagulating knife blade does not become hot and can be removed from boiling cervical tissue and touched with the bare hand with nothing more than a slight sensation of warmth. All of the heating with electrocoagulation is within the cervical tissue itself, it is heated from within out, complete, instantaneous coagulation and complete destruction following. Air is excluded, as the coagulating knife blade is not on the surface but is buried within the tissue and kept there, hence there is little or no oxidization and little or no scar tissue produced in the healed cervix. Histologic sections following coagulation in a limited number of cases showed the surface covered with squamous epithelium and no scar tissue was microscopically recognizable. Further studies are being pursued to prove this advantageous point over the Sturmdorf operation.

We wish to state this essential difference most emphatically and give it as one of the chief reasons why it is possible to remove the cervix surgically by the coagulation method and obtain a good anatomic result. The analyses of 125 cases of cervicitis treated by the coagulation method shows that stratified epithelialization was complete in an average of five weeks; anatomic closure of eversion was complete in five weeks, and the duration of bloody discharge after treatment (no hemorrhage) was two weeks. There was cessation of mucopurulent discharge in six weeks. Four cases of hemorrhage required packing. Only one of these patients

with postoperative hemorrhage remained in bed following treatment, as directed. There was no case of stenosis requiring operative treatment and no instance of pelvic peritonitis or cellulitis.

Dr. Cherry of the New York Post-Graduate Medical School endorses coagulation of the cervix for the treatment of cervicitis in no unreserved terms. He uses an intracervical electrode which does not bury itself within the tissue and the coagulation takes place between two metal strips, or between two needle points. He claims for his method a definite limitation in depth of coagulation and says that the procedure is particularly adapted to endocervicitis. He states that extensive cases of cervicitis often require several coagulations over a period of from two to three months.

It is our opinion that limited depth of coagulation is not sufficient to reach extensive cervical pathology, nor is the pathology concentric within the endocervical canal, but is eccentric and requires a varying depth of coagulation removal. This same criticism can be made of the Hyams cutting technic in which a wire loop on an insulated rod is spun about in the cervical canal, with a cutting current to cone out the cervical lesion that requires removal. By way of a homely illustration, the methods of Cherry and of Hyams resemble the old apple corer, which removes in a clean manner the apple core but cuts through a worm, leaving half of it within the apple tissue.

Our experience with a limited number of cases, using both the Ende-Cherry and Hyams instruments, would seem to bear out these theoretical objections. However, our experience with both the Hyams and the Ende-Cherry technics was in a limited number of cases, about 15 in all.

#### CONCLUSIONS

Medical heat per se does not produce cures of pelvic infection in the presence of chronic cervical pathology.

Chronic cervicitis associated with adnexitis and cellulitis is just as much a focus for reinfection as the cervix that harbors the gonococcus.

The treatment of chronic cystic cervicitis by means of surgical heat (electrocoagulation) has markedly increased the cures of associated pelvic infections.

Coagulation removes tissue subjected to chronic irritation, and the latter is a conceded factor in the etiology of cervical carcinoma.

Electrocoagulation resulting in a minimum of scar tissue bids fair to supercede the Sturmdorf operation.

Electrocoagulation may also be used for complete amputation of the cervix.

The simplicity of coagulation greatly increases its field of usefulness.

In the patient requiring hysterectomy where the supravaginal operation is preferred for lessened operative risk, deep coagulation of the cervix, either some weeks before or after operation, is recommended.

We have shown by studies of biopsies of chronic cystic cervicitis with erosion before treatment and after electrocoagulation, that electrocoagulation completely destroys the cervical glands, leaving a normal appearing stroma, and that the squamous epithelium grows down over the amputated cervix in a normal manner without "dipping" down irregularly into the stroma.

BEAUMONT MEDICAL BUILDING.

## A CRITICAL STUDY OF THE TECHNIC AND CLINICAL VALUE OF THE SEDIMENTATION RATE IN GYNECOLOGY\*

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THE sedimentation test as applied to gynecologic patients has been used for a number of years, both in this country and abroad. It has found relatively less favor here. Its proponents in this country are Polak, Baer, Reis, and Mathieu.

The purpose of this investigation was to determine:

1. What factors in connection with the routine performance of this test influence the sedimentation rate of red blood cells under the conditions of the experiment.
2. Are the claims correct as to the clinical value of this test.

### TECHNIC

At present there are many methods for determining the sedimentation rate. We investigated several of the more common technics. We avoided any modification which might make our results incomparable with those of other workers. As a preliminary measure a series of bloods were studied, comparing the Linzenmeier and Fåhræus method and some of their modifications. We chose the Westergren technic because of its speed, accuracy, and simplicity. The tests in this report were all determined by this method. All tests were done personally. We used a rack of our own design that held twelve of the special Mathieu pipettes. In collecting our samples, we used small 20 c.c. bottles and potassium oxylate for anticoagulant. Mathieu and his coworkers, found on testing 250 normal nurses that the normal sedimentation rate should be 15 mm. in forty-five minutes. Our findings tally with his. All our readings were made at fifteen and forty-five minute intervals. However, from our tests, we feel that the fifteen minute reading was of little or no value. The results shown in this paper are the number of millimeters of sedimentation at the end of forty-five minutes.

In order to determine what factors in the technic of the test might influence the rate of sedimentation of erythrocytes, several experiments were made.

I. Blood was withdrawn from the brachial artery and cubital vein at the same time and a test run on both samples under identical conditions. The variations in rate of 15 cases ranged from 4 mm. to 30 mm. with an average of 14 mm. The venous blood gave a uniformly higher rate than the arterial blood. The explanation of this is not apparent. We drew venous blood on 10 cases before and after producing a marked venous stasis. There was a variation in rate range from 3 mm. to 40 mm. with an average of 19 mm., which we attribute to the stasis. This variation was most marked in cases showing high sedimentation rates.

\*Read before the Chicago Gynecological Society, December 18, 1931.

II. We next tried the effect of rapid and slow withdrawal of blood from the vein. For this purpose blood was withdrawn from a large vein which was easy to enter and from which the blood flowed easily into the syringe and from a small vein of the same arm. On running the tests discrepancies as high as 50 per cent were noted, the blood being drawn by one of us (Summerville). When the blood was withdrawn from veins of equal size but by experienced and inexperienced individuals (senior students) the results on fifteen cases varied between 6 mm. to 87 mm. We attribute this to the partial coagulation of the blood, due to delay in mixing the blood with the anticoagulant. Plass claims that this source of error can be partly eliminated by drawing the blood under oil. We have tried his suggestion in several cases but find that if the difference in the time element in the withdrawal of the blood is maintained the discrepancies in the sedimentation rate still existed.

III. We next tried the effect of putting the anticoagulant into the syringe where it would mix with the blood as soon as withdrawn from the vein. One cubic centimeter of the 1 per cent solution of potassium oxylate was used for this purpose. This method was discarded because it was found difficult to draw exactly 5 c.c. of blood due to the angle between the fluid level and the calibrations of the syringe, and also because of frothing. Obviously if more or less than 5 c.c. was withdrawn differences in dilution with the anticoagulant would result, which would seriously interfere with the rate of sedimentation.

In order to further test the effect of the anticoagulant on the sedimentation rate we tested a number of bloods with moderate and vigorous shaking of the bottle containing the anticoagulant immediately after putting in the blood sample. It was found that those thoroughly mixed settled most rapidly.

IV. In order to determine the effect of standing before running the test on the samples of blood drawn we took 25 cases and ran tests at various times after withdrawing blood. The results are shown.

No. of cases	Av. of original rate	Av. Rate end 2 hr.	Av. Rate end 4 hr.	Av. Rate end 6 hr.	Av. Rate end 8 hr.	Av. Rate end 10 hr.	Av. Rate end 12 hr.	Av. Rate end 24 hr.
25	67	66.5 mm.	61.2 mm.	58.5 mm.	50.2 mm.	48.3 mm.	36 mm.	2.5 mm.

It will be seen that the sedimentation rate decreased directly as the time. There was practically no sedimentation after standing twenty-four hours. If a given sample was run immediately after being withdrawn from the vein, then allowed to stand in the ice box for set periods and brought back to room temperature and re-run it would give approximately the same sedimentation rate reading as controls that had been kept at room temperature.

In bloods that had been allowed to stand for 10 to 15 minutes after thoroughly mixing with the anticoagulant it was found that considerable variation in sedimentation rate occurred in samples taken from the upper and lower strata of the sample to be examined. The rate was always faster in the upper layer samples.

V. In order to test the effect of temperature change 25 samples of blood were run at room temperature and at 60°, 50° and 36-40° F. The sedimentation rate slowed down in direct proportion to the drop in temperature. There was very little change between room temperature and 60° but below this there was a decrease in rate. The average rate of 25 cases at 70° F. was 43 mm.; at 68° F. 39 mm.; at 50° F. 35 mm.; and between 36° to 40° F., 26 mm.

VI. Another source of variation in the sedimentation rate was found to lie in the length of the column of blood tested. When variations from the standard 200 mm. column were made, marked variations in the sedimentation rates were noted. Thus if the column were only 100 mm. long there was noted a difference of 23 per cent in the sedimentation rate in a series of twenty-five cases.

We did not find a constant ratio between the rapidity of the descent of the cells and the duration of time. Often the cells would settle very slowly at first, gaining momentum after from ten to twenty minutes and have about the same readings as a sample in which the cells settled very rapidly at first and then more slowly. It has been claimed that the rate of sedimentation is in inverse proportion to the number of red blood cells. We could not confirm this finding. There was no relationship between the gynecologic pathology and the sedimentation rate of the cells.

It is common in many gynecologic clinics, to insist that a patient should not be operated upon until the sedimentation rate reaches a normal level. Our results in 201 operative gynecologic patients do not support this view. On being admitted to the hospital, a careful history was taken and a thorough physical examination and laboratory work, was done on all cases. Sedimentation rates were run on these cases at frequent intervals, from one to eight tests being run on each patient. As soon as the patient appeared to be a good operative risk according to the history, physical findings, temperature curve and leucocyte count, she was operated upon regardless of the sedimentation rate. Almost all cases had a rate run on the day of the operation, and this rate is the one

TABLE I  
TABLE BRIEFLY SHOWING RESULTS ON OPERATED CASES

NO. OF CASES	DIAGNOSIS	NO. @ COMPL'S	SEDIMENTATION RATE			POSTOPER. HOSP. DAYS		
			LOW	HIGH	AVERAGE	LOW	HIGH	AVERAGE
12	Chr. Salp.	2	5	15	11-1/6	12	22	16-1/6
51	Chr. Salp.	5	15	121	41-5/51	10	22	13-32/51
11	Fibroids	1	6	15	12-5/11	10	16	13-1/11
49	Fibroids	6	16	128	50-1/2	10	34	13-1/7
13	Cyst. & Rect.	2	6	15	10-1/3	10	26	15-11/13
17	Cyst. & Rect.	3	17	44	28-14/17	10	29	17-2/17
1	Retro-Flex.	1	14	14	14	18	18	18
4	Retro-Flex.	1	18	32	25-3/4	12	18	15-1/2
5	Hyperplastic	1	8	15	12-2/5	7	28	13
6	Endometritis	0	16	84	36	4	18	9-2/3
3	Cystic Ovary	1	11	13	12	17	30	21-2/3
7	Cystic Ovary	1	16	114	70-5/7	10	16	13-6/7
2	Bicor. Uterus	0	18	31	24-1/2	14	14	14
1	Ca. of Cervix	0	11	11	11	4	4	4
3	Ca. of Cervix	0	57	80	68-1/3	4	14	12-1/2
1	Incomp. Abort.	0	12	12	12	11	11	11
2	Incomp. Abort.	0	24	36	30	5	7	6
12	Miscellaneous Cases	2	10	128	38-5/6	3	15	10-1/2

\*Rate readings given are those taken at the end of forty-five minutes. The normal sedimentation rate being 15 mm. in forty-five minutes.

considered in our averages. A total of 250 cases were studied and 201 patients were operated upon according to this procedure. Of this number only 48 had a normal or below normal reading. The remaining 153 showed an average sedimentation rate reading of 47 mm. in forty-five minutes in comparison to the normal rate of 15 mm. in forty-five minutes. This series consisted of the average run of gynecologic patients taken into the Research Hospital and the Cook County Hospital. The condition of the patient before and during the operation, the immediate postoperative condition, the postoperative course, the postoperative complications, and the number of postoperative days in the hospital of each was observed and compared. We found it practically impossible to distinguish among these patients between those having a normal or below normal reading and those having high readings.

There was very little difference as to the number of postoperative hospital days in each group. It was worth noting that frequently a patient would give a normal rate but was not considered a good operative risk according to the clinical and physical findings. It would have been interesting, but hardly justifiable, to have operated upon these cases.

Sedimentation rates were run on many of these patients postoperatively. They were always high. We found the rate highest about twenty-four hours after the operation. In most patients the rate began to fall after about three days often reaching a normal level by the end of the first week. However, in some patients, the rate remained persistently high for as long as ten days before it began to become lower and during this time the patient had an uneventful postoperative course. We found that in any complication such as acute bronchitis, hematoma, peritonitis, wound infection, evisceration, etc., there was a varying increase in the sedimentation rate. However, these complications were always self-evident, and we could see little diagnostic value of the rate here.

Doctors Henry and Herbert Schmitz, ran a series of 39 operative cases using the Linzenmeier technic which had a rate reading of sixty minutes or less. The normal reading by this technic being given as from 130 to 370 minutes. All had a normal recovery except one patient who developed a pelvic cellulitis. From their work they came to the conclusion that the sedimentation test was of no value in determining the safe operability of pelvic inflammatory conditions. We ran a series of 12 tests by this method and by the Westergren technic so as to get a comparison. The results tallied very closely.

#### COMMENT

It would seem from the above findings that there are many factors that may influence the sedimentation rate in gynecologic patients. From a practical point of view it would seem that the test is weak from the following reasons:

1. Because marked variations occur when blood samples are withdrawn by experienced and inexperienced people, or by the same person varying the time taken to withdraw the blood.

2. That, blood examined by this technic must not be drawn longer than two hours before the test is run.

3. Blood which has been kept in the ice box must not be used until it has been brought to room temperature.

4. The blood must be drawn to the same height in the pipettes in order to get equivalent readings.

5. If the samples of blood were not shaken for at least a minute, after removing the blood from the vein, marked variations in the sedimentation rate were noted. Most descriptions of the technic ignore this important source of error.

6. Because of the results in this series in which 250 gynecologic patients were examined and 201 operated upon and an additional 84 obstetric cases were studied, we feel that the test is of little or no value. This conclusion is based on the fact that in 153 cases, the operation was done when it was distinctly contraindicated by the sedimentation test but indicated according to the clinical findings, temperature, and leucocyte count. There was no mortality in these cases that could be attributed to infection following operation such as septicemia, pelvic abscess, or general peritonitis. Postoperative morbidity, complications, and hospital days did not vary from that of 48 operative cases with normal or subnormal sedimentation rates.

#### CONCLUSIONS

1. Many factors inherent in the technic tend to vary the rate of sedimentation of red blood cells as determined by the Westergren method.

2. There was no correspondence between the rate of sedimentation and the pathologic findings at operation.

3. The sedimentation rate was of less value than the ordinary clinical factors such as temperature, leucocyte count, and pulse rate in determining whether or not a patient should be operated upon.

4. Great economic waste would result from the application of this test to determine the time for operation.

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(For discussion, see page 455.)



# A SIGN FOR THE DETECTION OF SMALL AMOUNTS OF FREE BLOOD IN THE ABDOMEN\*

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THE specialty of gynecology has yielded the largest number of methods for detecting the presence of free blood in the abdomen, for which extrauterine pregnancy especially has furnished the incentive. Traumatic or spontaneous rupture of the spleen, rupture of an aneurysm, or other causes of hemoperitoneum are of such relative infrequency that these are not of much aid in studying the question. An accurate history and physical examination stand above all so-called pathognomonic signs yet described. It is quite evident that the authors who have described certain clinical phenomena or syndromes have not intended that these signs supply short-cuts to or absolute evidence for a diagnosis of such a condition as ruptured ectopic pregnancy. Instead, they have intended, that their test if present serve simply as confirmative evidence.

The truth of the latter statement is evident when we consider the occurrence of the following described objective or subjective findings in relation to hemoperitoneum.

Cullen's or by some called Hofstaetler, Cullen, or Hellendahl sign<sup>1</sup>; a bluish green or black discoloration of the umbilicus, ascribed to blood being visible through the overlying skin of this region, was recorded as being present in 6 of 1410 cases of extrauterine pregnancy.<sup>2, 3, 4, 5, 6, 7, 8</sup> This color change has also been ascribed to phlebectasia of the umbilical veins, indicating thrombosis of the tubal veins for, after the tube ruptures, the color has been said to disappear. Gold<sup>9</sup> reports discoloration present in 4 cases of hemoperitoneum which were associated with umbilical hernias. For the same reason it has also been suggested that the same color change could be noted in inguinal and crural hernias. Hanak<sup>10</sup> observed blue color of a scar for diastases recti in a case of hemoperitoneum. Busch<sup>11</sup> observed a bluish umbilical cyst with free blood in the abdomen. This same umbilical discoloration has also been described in association with acute hemorrhagic pancreatitis by Johnston,<sup>12</sup> Moynihan,<sup>13</sup> Turner,<sup>14</sup> and Bailey.<sup>15</sup> Ransohoff<sup>16</sup> found it in a case of rupture of the common bile duct.

Shoulder pain with hyperesthesia and hyperalgesia of the cutaneous distribution of the third, fifth, and especially the fourth cervical segments usually involves the right or left but occasionally both shoulders. Rubin states that the pain is on the same side as the ruptured tube in that the blood extends along the "lumbar gutter." This subjective and objective symptom is recorded by Robinson<sup>8</sup> as being first described by Oehlecker. In an analysis of 1105 cases of ectopic pregnancy, this symptom was noted as being present 87 times. Taking into account that relatively few cases reach the point where there is sufficient blood in the abdomen to extend up to the diaphragm the sign is fairly frequent. Also it must be kept in mind that unless the patient is questioned she may not volunteer this information. Capps<sup>17</sup> from his experiments of irritating the diaphragm concludes that phrenic nerve stimu-

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\*Read at a meeting of the Chicago Gynecological Society, December 18, 1931.

lation of the central or median portion of the diaphragm results in afferent impulses along the phrenic nerve which are distributed to the efferent third, fourth, and fifth cervical segments. Cope<sup>18</sup> has shown that this shoulder pain is present in the organs supplied by the phrenic nerve; namely, in diseases of the liver, stomach, diaphragm or its serous surfaces, duodenum, pancreas, spleen, gall bladder, pleura, or pericardium. In addition he maintains that the pain will be located in the supraspinous, acromial, or acromiodeltoid regions depending upon which region of the diaphragm is irritated. Shoulder pain is also a frequent and diagnostic sign in air injections of the fallopian tubes when they are tested for patency.

Laffont<sup>19</sup> noted extrapelvic referred pain which was located in the epigastrium, infracostal region, shoulder, retrosternal, interseapular regions, and in the base of the neck in 16 cases where the abdomen was filled with blood.

The character of the abdominal pain has been described as mild when due to repeated small hemorrhages into the peritoneal cavity. The colicky type of pain has been ascribed to tubal contractions. Whereas severe pain of a ripping, tearing, or bearing-down nature has usually been noted when there is considerable amount of free blood in the pelvis or abdominal cavity.

Culdesac bulging and tenderness are textbook findings and are frequently sought for immediately. Pain on manipulation of the cervix is regarded as important by Polak and Banki. Dyspareunia is simply another manifestation of the same symptom.

Urinary symptoms such as anuria, frequency, and dysuria, in reviewing 697 cases from three authors, were present on an average of 28 per cent. By some this is regarded, not as an evidence of nephritis, but as a result of the decreased blood pressure, associated with the hemorrhage, with inability of the glomeruli to serve as filters. However, these urinary symptoms are frequently present long before there are evidences of internal hemorrhage and frequently when only small amounts of blood are found in the abdomen. This is more likely a manifestation of irritation of the bladder peritoneum!

In 36 of 530 extrauterine gestation cases, painful defecation was recorded, undoubtedly due to pull on the pelvic peritoneum. From a diagnostic standpoint, however, this symptom is not pathognomonic as it may be present in inflammatory conditions of the pelvic organs.

Shifting dullness, if positive, proves the presence of large amounts of free blood in the abdominal cavity. Pallor, rapid pulse, decreased hemoglobin content and erythrocyte count, air-hunger and fainting are also evidence of an extensive hemorrhage and are recorded in all the textbooks.

Jaundice, a positive Van den Bergh, and elevated icterus index are not constant as shown by Horowitz and Kuttner.<sup>20</sup> Leucocytosis and elevated temperature are not of particular significance. The pyramidon test for hematin in the blood serum has been reported as being present in a large percentage of cases of ectopic pregnancy associated with free blood in the abdomen. Apajalahti,<sup>21</sup> however, in 32 cases of extrauterine gestation and 430 patients with other gynecologic conditions reached the following conclusion: the test is almost always positive in cases where the extrauterine gestation has been interrupted for more than one week and it is sometimes positive in parenchymatous and external bleeding. He obtained a positive reaction in cases of twisted ovarian cysts, carcinoma of the uterus, necrotized submucous myomas, intrauterine abortions, and in salpingo-oophoritis. He followed the technique given by Iwanoff.<sup>22</sup>

The presence of acetone in the urine cannot be relied upon, as evidence of hemoperitoneum, because acetonuria occurs in many other conditions that result in intestinal putrefaction.

By correlating all the above clinical manifestations indicating peritoneal irritation, namely: painful defecation, pain on manipulation of

the cervix, urinary disturbances, lower abdominal and later high abdominal pain, thoracic and shoulder pain, we are led to the following deductions. Early in the process of bleeding from an extrauterine pregnancy, the blood first irritates the pelvic peritoneum with concurrent local involuntary or induced pain. Upon ascent of the free blood the upper abdominal peritoneum is irritated with corresponding pain which may also be referred into the epigastric, retrosternal, mammary, or infracostal regions. With extension of the blood to the diaphragmatic surface the sensory fibers of the phrenic nerve are irritated with resultant referred pain in the shoulder region. In other words with the shifting of the "foreign fluid" there has been a corresponding "shifting" of the pain. This is well evidenced in a case of ruptured ovarian pregnancy described by Riches.<sup>23</sup> This patient obtained relief from the shoulder pain by assuming the sitting position which permitted the blood between the liver and diaphragm to gravitate to a lower level in the abdomen. Another example of produced shifting of peritoneal irritation is the following. Shoulder pain following the tubal insufflation of air is relieved by shifting the free intraabdominal air into the abdomen by elevating the lower part of the body. Dewes<sup>24</sup> made the following observation on a patient who had a large intraabdominal hemorrhage. The patient lying on her back had distinct shoulder pain which was relieved by pressing on the abdomen. His explanation was that the pressure forced the liver against the diaphragm and squeezed the blood from this region.

It is generally agreed that it is easy to diagnose the occurrence of a ruptured extrauterine pregnancy when the abdomen is filled with blood and all the signs of an extensive internal hemorrhage are present. To detect the presence of an unruptured tubal pregnancy has not been so easy until the introduction of the Aschheim-Zondek test for pregnancy. However, here we must not be led astray because the chorionic tissue may have been dead for some time, which results in a negative test.

The period of greatest diagnostic difficulty occurs when there are small amounts of free blood in the pelvis following the rupture of the tube, for it is at this point that all the above mentioned evidence of pelvic peritoneal irritation confuse the diagnosis and as these may be due to other causes, such as inflammatory conditions.

At this stage we may take advantage of the new sign. By shifting the free blood in the abdomen the following simple bedside test is obtained. Usually at this stage the patient localizes her pain in the lower abdomen, either to the right or left of the midline or occasionally in the suprapubic region, and usually there is corresponding tenderness and slight muscular rigidity. If now the patient is rotated to the opposite side, from her back on to the iliac crest, it will be observed that the subjective and objective symptoms have shifted to the dependent portion of the lower abdomen after a period of five to ten minutes. In other words,

concurrently the position of the blood and the region of peritoneal irritation have been shifted.

As to whether a positive shifting test will be a common occurrence, or very rare, it is impossible to say, but we shall expect to find it only when there is: free blood in the abdomen and not when all of it has formed a clotted mass in the pelvis which is adherent to the peritoneum. Nor can we expect a shift in the findings when the entire peritoneum is irritated by an abdomen full of blood, or when there is such a small amount of blood that it cannot be shifted.

Undoubtedly the previously described signs have occurred more frequently than is recorded, and frequently the history and physical examinations are not adequate and the signs are not sought for. Regardless of the absence or presence of any of the many diagnostic phenomena which have been described, they must be taken and interpreted as part of the entire picture in order to avoid mistakes in our diagnosis.

Only the essential facts bearing upon the subject of discussion are given in the two following cases.

CASE 1.—Patient, white, twenty-six years, had a spontaneous normal delivery four years previous, and eighteen months prior to her present condition she gave birth to a dead full-term infant.

Menses were regular, every twenty-eight days, five days' duration and unaccompanied by pain. Her last menstrual period ended seventeen days before the onset of the present condition.

On arising this day she noted slight "spotting," which in about one-half hour was followed by dull aching suprapubic pain which became severe in the next thirty minutes. Relief was obtained by rest in bed and in the afternoon she was able to be up and about, but with more or less discomfort. Later in the afternoon she felt "all-in," the pain increased, and extended over the lower abdomen but was slightly more marked in the right abdominal quadrant.

Physical examination, in the home, fourteen hours after the onset of the symptoms revealed the following essential findings:

Pulse 84, respiration 18, temperature 99°. Lying on her back the abdomen was slightly tender and rigid over the lower portion of the recti muscles, especially on release of pressure. No percussable dullness was present in the flanks.

Vaginal examination demonstrated no evidences of previous or recent infection nor were there any findings of pregnancy. The cervix was large, firm, not blue, but presented a red-velvety 3 to 5 mm. wide "erosion" that did not bleed on manipulation. The corpus uteri was of normal size, moderately firm, and only slightly tender on moving it. The culdesac and lateral fornices were rather tender but no distinct masses were palpable.

After examination there was considerable doubt as to what the underlying pathologic condition was, in view of a normal menstrual cycle, no mass to either side of the uterus, no findings of pregnancy, and her appearance was such as not to lead one to suspect the possibility of an intraabdominal hemorrhage. Because of this uncertainty as to the condition she was reexamined ten minutes later. At this time she was lying on her right side to which she had turned following the previous pelvic examination. Now the tenderness and rigidity were located over McBurney's point rather than in the suprapubic region. The shift in physical findings immediately gave the clew as to the possibility of free intraabdominal fluid that irritated the peritoneum. These same findings were displaced to the left lower quadrant by rolling the

patient to her left side. The conclusion reached was that she was bleeding internally, either from a ruptured corpus hemorrhagicum or from an extrauterine pregnancy. Operation was advised and consultation was requested after reaching the hospital. The consultant favored a diagnosis of appendicitis so the patient was given morphine, and ice bags were applied to the abdomen, and it was decided to operate in the morning. The operation consisted of the following procedures, in their order: dilatation and curettement, and amputation of the "eroded" cervix. Upon incising the peritoneum a large amount of unclotted dark blood spurted from the abdomen. In the pelvis was a moderate amount of recently clotted blood. The right tube was normal and the right ovary cystic. The left tube was very slightly thickened and blood was pouring forth from the fimbriated end. No fetus was found but microscopic examination of the tube showed chorionic villi. The left tube, right ovary, and appendix were removed.

CASE 2.—Patient, white, twenty-five years, 2 previous spontaneous normal deliveries, the last nine months previous to present condition. Her menses began five months after the latter delivery, had not become regular since in that they were at five to six week intervals. For six weeks prior to the onset of the below symptoms she had used a rubber-diaphragm and a contraceptive jelly every time she had had intercourse. Her last menstrual period was as usual and of four days' duration. Thirteen days following the termination of this last menstrual period she developed the following complaints. On this day she had an attack of lower abdominal pain which occurred at irregular intervals. It was of a cramping or colicky nature at first but later was described by her as feeling as though ground glass was being rubbed in the lower abdomen.

Six hours after the onset of the above complaints she was examined, at the home, and presented the following findings: Temperature 98°, pulse 80, and respiration 18. Slight tenderness and practically no rigidity were present in both sides of the lower abdomen. Shifting her body increased the pain over the most dependent portion of the lower abdomen, as in Case 1.

Vaginally, to the right of an anteverted and normal sized uterus was a 4 by 3 cm. tender mass. The culdesac was bulged slightly and was tender on digital manipulation. No evidences of pregnancy, or infection were present. Hospitalization was advised, however, the patient's condition seemed nonurgent so that she did not arrive until five hours after she was seen in her home. "Faintness" had been complained of on 2 occasions on her way to the hospital. On entrance the shifting-test was now negative. She complained of epigastric and infracostal persistent aching pain which to a certain extent overshadowed her right shoulder pain. By this time the rigidity and tenderness were more marked in the lower abdomen and especially in the culdesac. The hemoglobin reading was 75 per cent and the red blood count 3,890,000, and the leucocyte count 18,900 with 81 per cent polymorphonuclear leucocytes. Pallor was definitely apparent at this time. Several attempts at urination failed but catheterization, preoperatively, yielded about six ounces of urine.

*Operation.*—Upon incision of the blue gray peritoneum a large amount of dark clotted and unclotted blood "welled-out" from the wound. Both tubes, and left ovary were normal. The uterus was of normal size, freely movable and anteverted. The lateral pole of the right ovary was the site of a bleeding intrafollicular type ovarian pregnancy.

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4627 KENMORE STREET.

(For discussion, see page 457.)

## COMPLETE TRAUMATIC AND SPONTANEOUS INTRAPARTUM RUPTURES OF THE UTERUS. A REPORT OF THREE CASES WITH NO MATERNAL MORTALITY, AND ONE LIVING CHILD REMOVED FROM THE ABDOMINAL CAVITY FORTY MINUTES AFTER THE UTERINE RUPTURE

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**I**NTRAPARTUM rupture of the uterus constitutes one of the tragic accidents that occur in obstetric practice. This catastrophe may be avoided if the attending obstetrician is conversant with the conditions which predispose to its occurrence and recognizes in due time the ever present objective and subjective signs and symptoms that forebode its onset.

CASE I.—E. B., aged thirty-five years, para ii, the last labor seven years ago. Both labors were instrumental. Last period occurred on February 16, 1917.

On October 26, 1917, I was called to the patient's house. The patient had been in labor for sixteen hours, the membranes having ruptured at the very onset. Although a diagnosis of transverse presentation was made by the attending obstetrician, the labor was permitted to continue unaided. I found a right posterior shoulder presentation with the right hand and pulsating umbilical cord protruding from the vagina. The uterus was tightly contracted, and Bandl's contraction ring very plainly seen at a much higher level than usual.

Much against my desire and clinical judgment, I yielded to the entreaties of the family to deliver at home by version of the still living child. Under deep ether anesthesia I performed a podalic version and succeeded in delivering the body of a large child, but could not extract the head. I decided to do a craniotomy, but found the body to be in the way; so I severed it at the base of the skull. On attempting to apply the forceps to the severed head, it suddenly disappeared from view, and a vaginal examination disclosed to my great dismay, a deep rent in the left lower uterine segment, through which the head had slipped out into the abdomen. The child weighed 11 pounds.

The vagina was packed with iodoform gauze and the patient transferred immediately to the Sydenham Hospital, and directly to the operating room.

*Operation.*—The peritoneal cavity contained a moderate quantity of free blood, about eight ounces, but no active bleeding from the tear in the uterus. The tear was complete and extended from the level of the internal os upward to near the insertion of the round ligament. The amputated head and the placenta lay free in the abdominal cavity above the fundus uteri. (Fig. 1.) After removing the fetal head and

the placenta I performed a supracervical hysterectomy, and drained through the dilated cervical canal. The recovery was uneventful and the patient left the hospital at the end of two weeks.

CASE 2.—L. S., aged thirty years, primipara. Last period terminated on December 12, 1921. Estimated date of delivery September 16, 1922.

On July 15, 1922, following an automobile accident, the membranes ruptured, and mild labor pains set in which lasted but a few hours.

On August 1, 1922, labor pains set in again, much stronger in character than in July, and when the attending obstetrician arrived at the patient's home, he found a pulsating umbilical cord protruding from the vulva. The patient was transferred to the Beth Moses Hospital, and an attempt to deliver with forceps was made. During the procedure the patient went into shock, and I was summoned.

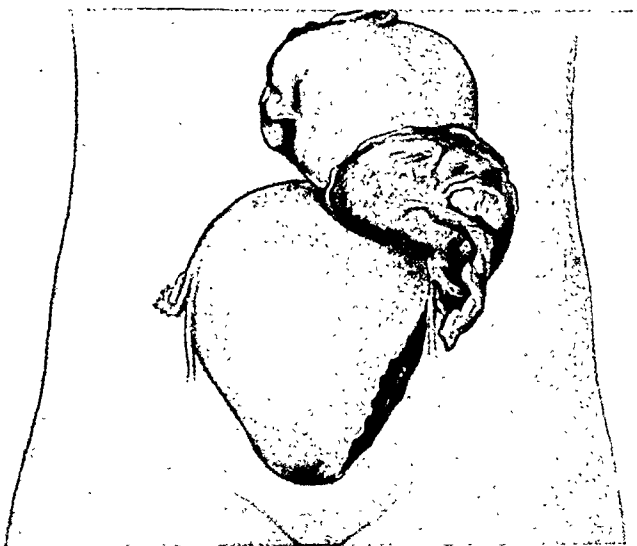


Fig. 1.—E. B., aged thirty-five years, in labor sixteen hours; transverse presentation (Sc.D.P.); right arm and umbilical cord prolapsed; version and severing of body at the base of skull; traumatic intrapartum rupture of uterus; escape of amputated head and placenta into peritoneal cavity through the uterine tear. Hysterectomy, recovery.

*Physical Findings.*—A well-built female, markedly anemic, ashen gray in color, with an anxious expression. Abdomen enlarged by a gravid uterus, corresponding in size to an eight months' gestation. The lower part was wider than the upper. Vaginal examination revealed free oozing of dark red blood, a tear extending from the inner surface of the right labium majus upward to and above the urethral opening. The portio vaginalis was not yet effaced, and the rim of the external os was still considerably thick and dilated to the width of four fingers. The back of the child was anterior, head to the right left shoulder impacted, and the left arm and umbilical cord in the vagina. On the left side there was a uterine tear, extending from the external os upward into the left uterine wall, through its entire thickness, so that the examining fingers could be introduced readily into the free peritoneal cavity. The uterus was firmly contracted over the child's body, and Bandl's contraction ring, running in an oblique manner, could be noted easily.

*Operation.*—A cesarean section followed by a supracervical hysterectomy was performed. Abdomen closed without drainage. The postoperative course was uneventful, excepting for a febrile course for the first three postoperative days. The patient left the hospital on the fourteenth day, feeling well.

CASE 3.—I. L., aged thirty-seven years, para xi. Last menstruation on June 19, 1930. Admitted to the Jewish Maternity Hospital on March 26, 1931, in labor.

After a prolonged but ineffectual endeavor, it was decided to terminate the labor with forceps. On March 27, at 8 A.M., the patient was anesthetized and the attending obstetrician, on examining the patient prior to the application of the forceps, discovered a fresh cervical tear on the right side, which extended to the base of the broad ligament. The contemplated forceps delivery was abandoned, and I was asked to see the patient.

On my arrival the patient was on the operating table, partly anesthetized. Inspection and palpation of the abdomen showed lax abdominal walls and an irregular tumor mass, consisting of two distinct parts, separated by a groove. The larger part occupied the upper two-thirds of the abdominal cavity, and corresponded in outline to that of a child's body; and the smaller part with the contour of a uterus in the fourth month of pregnancy, lay in the hypogastric area.

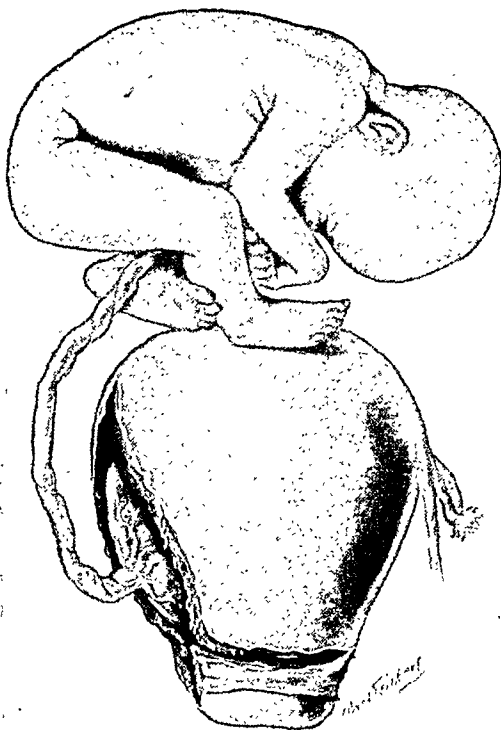


Fig. 2.—I. L., aged thirty-seven years, para xi, in labor twenty hours, pendulous abdomen, spontaneous intrapartum rupture of uterus with escape of the child into the abdominal cavity. Removal of a living child from the abdominal cavity forty minutes after the rupture. Hysterectomy, no drainage, uncomplicated recovery.

From the vaginal findings and the abdominal signs, a diagnosis of rupture of the uterus with the escape of the child into the abdominal cavity, was made.

*Operative Findings.*—A moderate amount of free blood in the peritoneal cavity, about eight ounces, and vernix caseosa. The living child lay above the uterus, with the umbilical cord attached to the placenta, which extruded partly through a rent in the right uterine wall (Fig. 2). On closer inspection it was found that the uterine tear on the right side began at the external os and terminated at a point below the insertion of the round ligament, and it laid bare the folds of the broad ligament as well as the outer leaf of the mesocolon, thus exposing the iliacs, the ureter and the muscles of the pelvis. The longitudinal tear was joined at the level of the cervico-uterine junction by another complete uterine tear which ran transversely from the left border of the uterus to the right.



*Operation.*—Laparotomy, extraction of a living child, hysterectomy, bilateral salpingo-oophorectomy, resuturing of the ascending colon to its outer peritoneal attachment, complete peritonealization of the pelvic floor, closure without drainage.

The postoperative course was uneventful, and both mother and child left the hospital at the end of the third week, feeling well.

1125 MADISON AVENUE.

## CARCINOMA OF THE BODY OF THE UTERUS IN CHILDHOOD

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(From the Clinic of Drs. McMullen, Lenz and McGauley)

IN A recent study of cancer of the uterus by Lane-Clayton,<sup>6</sup> the age of incidence is recorded from the five countries supplying the most reliable statistical data. Patients under thirty years of age made up 1.2 per cent of the total. The mean age of all patients was fifty-three and three-tenths years.

Cullen<sup>1</sup> in his exhaustive study of uterine cancer at the Johns Hopkins Hospital found only three patients thirty years or younger in his series. He warned that in estimating the age of these patients some latitude must be allowed, inasmuch as it is impossible to determine accurately just when the disease began, and it is safe to assume that in some patients the process had already existed from one to two years before an operation was undertaken.

Gusserow<sup>3</sup> in a study of 3471 cases found only one patient nineteen years of age, and 114 between twenty and thirty years of age.

Peterson<sup>9</sup> found that of 500 cases, 1.4 per cent occurred between the ages of twenty and twenty-five.

Stacy<sup>10</sup> reporting 333 cases of uterine cancer from the Mayo Clinic, operated between the years 1907 and 1923 found that 10.51 per cent of the patients were less than forty-five years of age, the youngest being nineteen years. He emphasized that carcinoma of the fundus of the uterus occurs in a fairly large number of women under fifty years of age; and that recent studies show a greater incidence in younger persons than was shown in earlier reports.

In a recent study on malignant growths of the uterus in young girls, Hirst<sup>4</sup> reported a case in a girl of fifteen years. He believes that malignant growths of the uterus in the very young are not so excessively rare. This case is included in the group under consideration, as it was undoubtedly a true case of malignant uterine tumor. A portion of the tumor was removed after cervical dilatation and examined microscopically. Because of the history of prompt recurrence of profuse irregular bleeding, following the removal of a cervical polyp five months previously, together with the definitely malignant features of the curettings, panhysterectomy was performed. This patient was alive and well ten months postoperatively.

Prior to the publication of Morse's paper<sup>8</sup> in April, 1930, on carcinoma of the female genital tract in childhood, I reviewed the literature to determine the incidence of uterine cancer in the very young, and reached similar conclusions; namely, that many of the previously

reported cases were incomplete, especially in regard to adequate study and description of the pathologic material.

Accepting the reports, Ganghofner,<sup>2</sup> Glöckner and Kehrler,<sup>5</sup> and adding the cases of Hirst,<sup>4</sup> and Morse,<sup>8</sup> we find a total of 5 authentic cases of uterine cancer in young girls below the age of fifteen years.

Great difficulty is naturally encountered in determining the exact histology and the true site of the origin of pelvic tumors in the female. It is well known that sarcoma is a frequent tumor of the very young, also that teratomatous tumors of the ovary are relatively common. Vestigial organs such as the wolffian duct, are a possible site of origin of such neoplasms developing from fetal rests. In fact, there is a large group of mixed tumors of congenital origin which make exact classification difficult.

Because of the above possibilities of error, the following case was studied by ourselves and tissue was forwarded to Ewing and Stewart of the Memorial Hospital, and Morse of New Haven for confirmation of the diagnosis.

*Case Report.*—J. C., aged eleven, student, admitted March 27, 1928, referred by Dr. R. A. MacTaggart, with chief complaints of vaginal bleeding, pelvic tumor, and slight abdominal discomfort. Family history negative for history of tumors or tuberculosis. The mother gave no history of miscarriages. Past history: measles, chicken pox, whooping cough, and several attacks of bronchitis. Present illness: began about September, 1927, with vaginal bleeding. This continued for about three days. The following three months the patient had regular vaginal bleeding, lasting from three to four days. In January and February no bleeding occurred. Patient admitted with vaginal bleeding, no pain. Complained of increasing pelvic tumor, which had grown rapidly in past three months. Physical examination negative, except for local condition in the abdomen and pelvis. Tumor mass approximately 12 cm. in diameter in bladder region of abdomen. Mass hard, immovable and not attached to skin. Vaginal bleeding determined by pelvic examination. Cervix appeared normal to visual and digital examination.

Operation, March 30, 1928, under ether anesthesia. Midline incision exposed irregular nodular mass approximately 12 cm. in diameter filling the pelvis and adherent to the bladder anteriorly. Fundal hysterectomy and right salpingo-oophorectomy. Left tube and ovary appeared normal and were left in situ.

Laboratory Report: (Ellis Hospital) by Dr. Ellis Kellert, March 30, 1928. The uterus measured approximately 4.5 cm. in diameter. At the point of incision the uterine wall was 8 mm. and apparently was on one tubal side. The opposite half of the uterus was replaced by a firm solid infiltrating tumor growth continuous with the endometrium. The tumor filled the endometrial cavity. Continuous with the growth in the uterus was a large irregularly nodular tumor mass 12 by 6 by 9 cm. and at its upper surface was a normal appearing tube. Cut surface of this growth and of the uterine mass showed a firm fibrous tumor structure studded and streaked with yellowish puncta. No ovarian tissue was identified. Near the surface of the tumor were several yellowish necrotic foci. The capsule of the growth appeared intact except at one point near the uterus. Malignant tumor involving endometrium, uterine wall and ovary. The growth occurred in the form of masses of undifferentiated tumor cells separated by thick fibrous strands. There was a distinct resemblance to epithelium. The

cells varied greatly in size, some being rounded, others elongated. Mitotic figures were rare.

Dr. Ewing reports: "The sections and radiograph of the tumor of the uterus in the girl of eleven are quite remarkable. The structure is more suggestive of a primary carcinoma of the uterus rather than a primary tumor of the ovary. Yet, primary tumors of the ovary are very much more frequent in children of this age than tumors of the uterus. The anatomy suggests that it has arisen in the uterus. Grade IV. Radio sensitive." (Fig. 1.)



Fig. 1.—High power photomicrograph showing anaplastic carcinoma, Grade IV. Radiosensitive.



Fig. 2.—Radiograph of chest taken seven months postoperatively, shows evidence of widespread bilateral pulmonary metastases.

Following hysterectomy, March 30, 1928, patient was referred for high voltage x-ray treatments when a complete pelvic cycle was administered. Chest plates taken October 27, 1928, showed extensive metastases throughout chest (see Fig. 2.) Patient died December 15, 1928, from chest involvement with no evidence of local recurrence. It was impossible to obtain an autopsy.

#### CONCLUSIONS

1. A total of 5 cases of carcinoma of the uterus had been reported to which we added the present case report.

2. Carcinoma of the uterine organs in childhood is of rare incidence, but should be considered in all cases of irregular bleeding in young girls.

3. Following the established diagnosis by means of biopsy or curettage, the mode of treatment should be surgical if the clinical setting allows for complete removal, or a combination of radium and deep x-ray therapy if the condition is inoperable. Because of the surgical difficulties in young children, radiation therapy is probably the method of choice.

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**Kermauner**: Treatment of Genital Tuberculosis in the Female. Wiener. Klin. Wchnschr. 43: 1245, 1930.

Genital tuberculosis comprises 1 to 2 per cent of all genital disease, and 10 per cent of all adnexal tumors. The author stresses the difficulty in diagnosis. Of 92 cases seen in his clinic a positive clinical diagnosis was made in only 32 cases. Laparotomy to assure diagnosis is strongly advocated. Numerous cases illustrating the difficulties encountered are presented.

Attention to the general health of the individual is of primary importance in treatment. X-ray is the procedure of choice where the diagnosis is certain. Small doses are used, 10 per cent E.D., three treatments at intervals of from one to three months. The amenorrhea produced appears to be beneficial. Operation is to be performed when the diagnosis is in doubt, and adnexa removed not as a therapeutic but a diagnostic procedure. Since most cases are secondary, hysterectomy has been discarded as unnecessarily endangering life.

FRANK SPIELMAN.

## CANCER PROPHYLAXIS\*

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**P**ATIENTS with cancer of the uterus comprise about 6 per cent of the average gynecologic service. In most of these cases, in spite of the best methods of treatment available, the word cure is but a relative term signifying freedom from disease for a comparatively short period of years. Confronted year after year by these tragic patients in whom treatment has failed, one is driven to demand what more can be done to prevent this pitiful procession which files through our hospitals today?

In an attempt to answer this question, we have reviewed the histories of 259 consecutive patients with malignant disease of the uterus occurring in the Hospital of the Woman's Medical College of Pennsylvania and in the Woman's Hospital of Philadelphia. My colleagues on the staffs of these two hospitals have generously allowed me to consult the records of their patients and to combine these with my own in making this report. I take this opportunity to express my appreciation of their courtesy.

These cases are grouped as follows:

Cancer of the uterine cervix	200
Cancer of the cervical stump	12
Cancer of the uterine body	42
Sarcoma	5
Chorioepithelioma	0
	<hr/>
	259

### CANCER OF THE CERVIX

Of the 200 patients with cancer of the cervix, 161 were white, 39 were negroes (19.5 per cent). The family history was positive for cancer in 18 per cent of the cases in which it is recorded (171).

The age incidence ranged from twenty-four to eighty-one, as shown in Fig. 1. The fact that 10 per cent of the cases occurred in women under thirty-five years of age and 20 per cent in women under forty years of age immediately arrests our attention.

Cervical erosions were reported in 13 cases. Cervical polyps were reported in 11 cases. Myomatous tumors of the uterus were reported in 10. Six patients gave a history of wearing a pessary. There was 1 case of procidentia. The Wassermann reaction was taken in 82 cases and was found positive in 8.

Of these 200 patients, 184 had been married, 15 were single (7.5 per cent), no record in one. One hundred and fifty-nine patients had had

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\*Read at a meeting of the Obstetrical Society of Philadelphia, January 7, 1932.

children or children and miscarriages; 12 had had miscarriages and no children; 26 were nulliparous (13 per cent); no record in 3. Thirty-two patients gave a history of instrumental deliveries.

Only 1 patient had had a cervical operation. This patient gave a history of cervical amputation and bilateral salpingo-oophorectomy in the Woman's Hospital eleven years before she was readmitted with squamous cell carcinoma of the cervix. The pelvic examination at the time of op-

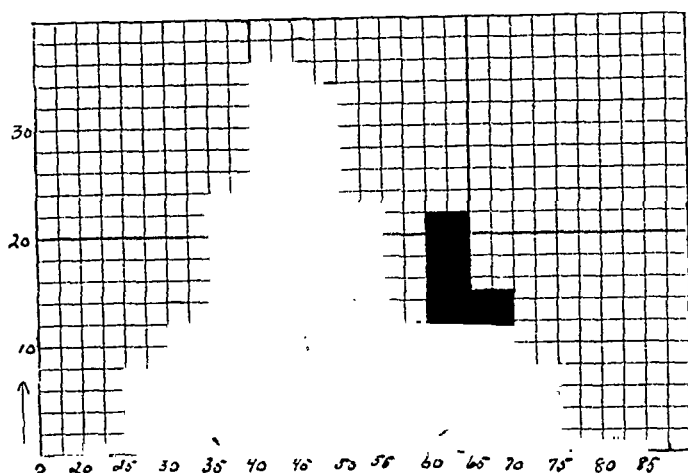


Fig. 1.—Age incidence in 200 cases of cancer of the cervix.

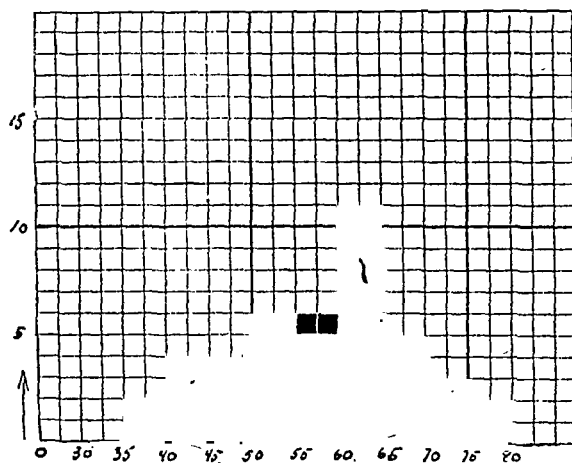


Fig. 2.—Age incidence in 42 cases of cancer of the fundus.

eration showed a bilateral laceration of the cervix with erosion. The curettings showed glandular hyperplasia, the cervix was not sent to the laboratory.

Twenty-six of these 200 patients were nulliparous (13 per cent). Seven of the nulliparous patients gave a history of cervical polyps; 4 gave a history of uterine myoma; 2 gave a history of cervical erosion. In other words, in the histories of all but thirteen (6.5 per cent) of the 200 cases of cancer of the cervix, childbirth, miscarriages or some form of epithelial irritation was recorded.

## CANCER OF THE BODY

Of the 42 patients with cancer of the body of the uterus, 39 were white; 3 were negroes (7 per cent). The family history was positive for carcinoma in 15 per cent of the cases in which it was recorded (33).

The age incidence ranged from thirty-five to eighty years, as shown in Fig. 2. Five per cent of these cases were in women under forty years of age.

Cervical erosion was present in 1 patient; cervical polyps were present in 6 patients; myomatous tumors of the uterus in 11. In 2 cases, cancer of the uterine body seemed to be secondary to malignant cysts of the ovaries. The Wassermann reaction was taken in 6 cases and found negative in all.

Of these 42 patients, 31 had been married, 11 were unmarried. Twenty had had children or children and miscarriages. Twenty-two had had no pregnancies (52 per cent).

## CANCER OF THE CERVICAL STUMP

Of the 12 patients with cancer of the cervical stump, 6 were white, 6 were negroes. The family history was positive for carcinoma in 1.

Three cases were the result of incomplete operations. In each of these a cancerous uterus had been removed by supravaginal hysterectomy one year before the patient was admitted to the Woman's Hospital with cancer of the cervical stump. In 1 case a supravaginal hysterectomy had been performed in one of the smaller hospitals of this city in April, 1924. The history states the removed uterus was a "fibroid showing beginning degeneration." There was no microscopic examination. Five months later this patient was admitted to the Woman's Hospital with a cancer of the cervical stump. This was probably due to an incomplete operation.

In 2 cases, supravaginal hysterectomy had been performed four years before the patients were admitted for cancer of the cervical stump. According to the patients' statements the operation had been performed in one instance for "ulcer of the womb," in the other instance for "fibroid tumor." One patient had been operated upon for fibroid tumor five years before admission. One patient had been operated upon for chronic inflammation eight years before admission. The others had been operated upon ten, thirteen, sixteen, and twenty-one years before admission. We were not successful in getting reports on the uterine pathology found in these cases at the time of operation.

Some of these latter cases may represent incomplete operations. The last 4 probably do not.

## SARCOMA.

Of the 5 patients with sarcomatous tumors, 4 were white, 1 was a negro. The family history was negative for malignancy in 4 patients, inadequate in 1. The Wassermann reaction was negative in 2 patients, not taken in 3. The age incidence was from fifty to sixty-five. Cervical

polyps were reported in 2 cases, myomatous tumors in 3. All 5 patients had been married and had borne children.

#### SUMMARY OF 242 CASES OF CANCER OF THE UTERUS

	CERVIX (200)	BODY (42)
White	80½%	93%
Negroes	19½%	7%
Age incidence	24-81	35-80
Positive cancer heredity	18% (of 171 cases)	15% (of 33 cases)
Cervical erosions	6½%	2%
Cervical polyps	5½%	14%
Myomatous tumors	5%	26%
Childbirths or miscarriages	87%	52%

This summary contains nothing new. It emphasizes certain well-known facts.

1. Cervical erosions appear to be a factor in the development of cancer of the cervix.

2. Cervical polyps appear to be a factor in the development of cancer of the uterus (cervix and body).

3. Symptomless myomas appear to be a factor in the development of malignant disease of the body of the uterus.

4. The traumatism of childbirth or miscarriage appears to be the most frequent factor predisposing to malignant disease of the cervix.

From these facts it seems logical to conclude that many cases of cancer of the uterus could be prevented by periodic pelvic examination and by the immediate repair of the lacerated cervix.

#### PERIODIC PELVIC EXAMINATIONS

The importance of these is apparent. In the course of such examinations, predisposing factors, such as polyps, erosions, lacerations, and myomas, may be detected or suspicious symptoms elicited and biopsy or diagnostic curettage performed.

The patients' natural reluctance to be examined can usually be overcome by carefully explaining why the examination should be made.

#### IMMEDIATE REPAIR OF THE CERVIX

If, as our series shows, 20 per cent of cancers of the cervix occur in women under forty years of age, the method of preventing cancer by repairing the cervix at the end of the childbearing period is inadequate.

From the standpoint of cancer prophylaxis there is no time like the present; immediate cervical repair is the method of choice. From the standpoint of the obstetrician this method is not yet popular. Two serious objections are raised against it: first, the possibility of carrying infection into the uterus; second, the possibility of nonunion because of the lochial discharge. Thirty-five years ago similar objections were raised against the immediate repair of the perineum.

In order to settle this matter for ourselves, we undertook the immediate repair of the lacerated cervix in all primiparae delivered on our service at the Philadelphia General Hospital during the past summer.



After delivery the cervix was carefully inspected, lacerations noted and repaired by the assistant chief resident physician or by the interne with the resident physician's help. General anesthesia, nitrous oxide, or ether was usually required. For exposing the cervix we used Jackson's right angled vaginal specula; for grasping the cervix we used Teale's forceps. Both silkworm and catgut sutures were given a trial.

This method entailed considerable extra work for the medical and nursing staff. Without their willing cooperation the experiment could not have been made. I take this opportunity to express my hearty appreciation of their help.

#### RESULTS OF IMMEDIATE REPAIR IN THIRTY-FOUR PRIMIPARAE

Thirty-two of the cases were vertex presentations; 25 of these were delivered spontaneously, 6 by low forceps, 1 by axis-traction forceps. Two were uncomplicated breech deliveries.

The laceration was bilateral in 20 cases, unilateral in 12, stellate in 1, type not stated in 1.

Chromic catgut was used in 25 cases, silkworm gut in 8 cases, catgut and silkworm gut in 1 case with practically similar results.

Good union was reported in 24 cases; nonunion, in 3 cases; one side united, one side not united in 6.

In 23 cases, the puerperium was afebrile. Eleven cases presented a slight febrile rise. In 2 cases the temperature rose to 99.6° F. In 6 cases a temperature of 100° to 101° F. was recorded on one or more occasions. In 1 patient the puerperium was complicated by a gonorrheal arthritis with a rise of temperature to 102.6° F. In 1 case, in which the episiotomy incision became infected, the temperature rose to 103° F. on the third day. One patient developed a gonorrheal salpingitis during her puerperium and ran a febrile course.

On the basis of these cases, the objections to immediate repair of the lacerated cervix would seem to be unfounded. If such good results can be obtained by a group of young doctors in Philadelphia, they can be duplicated or excelled in every well-equipped delivery room in this country.

In the campaign to prevent cancer, this method seems worth extensive trial.

#### CONCLUSIONS

1. The chief means available to prevent cancer of the uterus are periodic pelvic examinations and immediate cervical repair.
2. Immediate repair of the lacerated cervix is a safe procedure.
3. Immediate repair of the lacerated cervix was successful in 73.5 per cent of a series of 34 cases.
4. Prevention of cancer of the cervix is largely the obstetrician's opportunity.

## CLOSURE OF SMALL VESICO- AND RECTOVAGINAL FISTULAE BY MEANS OF DIATHERMY AND THE MONOPOLAR CURRENT

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*(From the Gynecological Service of the Mount Sinai Hospital)*

IN NOVEMBER, 1917, I reported the cure, by means of fulguration, of a minute vesicovaginal fistula which persisted after the closure of a large defect.<sup>1</sup> Since then, 3 more small, inaccessible vesicovaginal fistulae, the residua of otherwise successful operations, were closed by the same method. In all 3 cases, a difficult operative closure was avoided. It therefore seems worthwhile again to call attention to this simple technical procedure which occasionally proves of great value.

The method is applicable only to openings no larger than 3 millimeters. If the intervening vesicovaginal septum is extremely thin, closure cannot be hoped for. The bladder is distended by means of a continuous current of water introduced through one channel of a catheterizing cystoscope, the second channel containing the insulated wire electrode. The fistula is well visualized, the active electrode is introduced into the vesicle end of the fistulous opening for a very short distance, the large indifferent electrode being applied to the sacral region. The current is turned on only momentarily to freshen the fistulous tract. The electrode is then withdrawn and the mucosa surrounding the fistula is fulgurated lightly, never producing more than a superficial whitening of the surface, for a distance of 3 or 4 millimeters. It is essential not to char the tissues, otherwise the opening will be increased in size rather than diminished. In those cases in which the mucosa surrounding the fistulous tract is hypertrophic or edematous, a single application may be sufficient. Usually at least temporary closure results within twenty-four hours, due to the edema resulting from the cauterization. If the first treatment is not followed by permanent healing, an interval of from two to three weeks must elapse before a second attempt is made. Inspection through the bladder then determines the likelihood of successful closure. After three weeks have elapsed, the opening should be diminished in size. If so, the treatment may be repeated.

If the vesicovaginal septum is thick, the vaginal end of the sinus may be cauterized with the monopolar current to expedite the closure. Here, too, only very little sparking must be used.

The following case history illustrates the great value of this simple procedure.

M. L., forty-two years old, was admitted to Mount Sinai Hospital, February 25, 1931. Continuous leakage of urine followed a complete hysterectomy performed at another institution in 1930. Shortly thereafter attempted closure from below, at

the same hospital, proved unsuccessful. She was then reoperated upon, first by the vaginal route and later transperitoneally at another institution without relief. A ventral incisional hernia overlapping the pubis developed at the lower angle of the scar.

When I first saw the patient, a large obese woman, she was losing all her urine through the vagina. The canal was long, rigid, scarry, and distorted. At the apex of the vagina an opening, embedded in scar tissue, communicating with the bladder, could be visualized with difficulty. Cystoscopy (the vagina being blocked with a colpeurynter) showed a funnel-shaped opening  $1\frac{1}{2}$  centimeters long, about

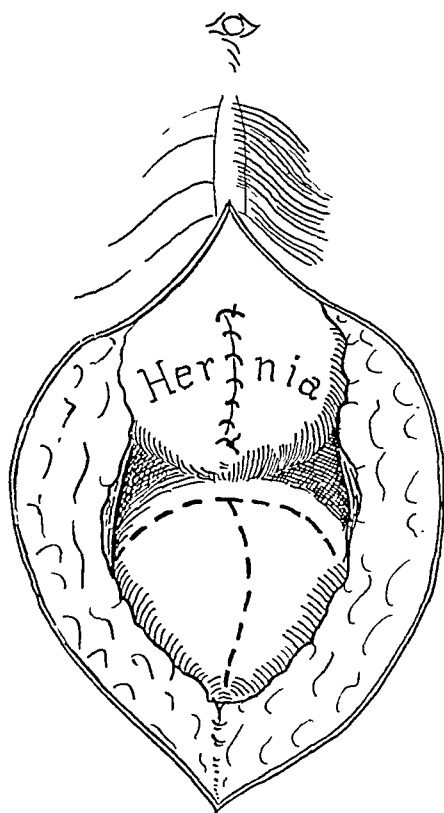


Fig. 1.

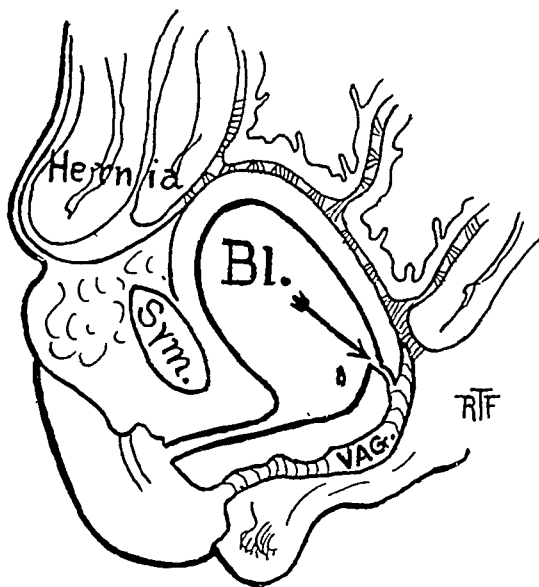


Fig. 2.

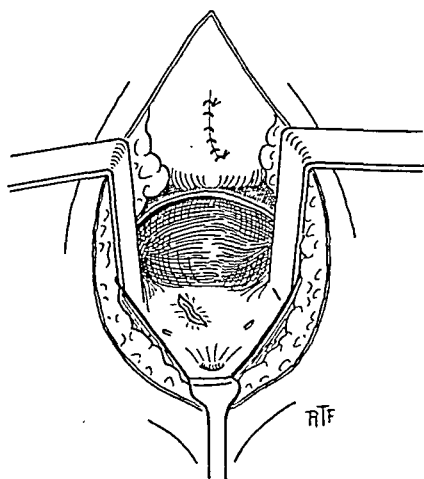


Fig. 3.

Fig. 1.—Ventral hernia overlapping bladder, showing peritoneum resutured. Posterior wall of bladder could not be freed. Broken lines indicate incision into the bladder. Below, catheter through urethra for distending bladder.

Fig. 2.—A schematic sagittal section of pelvis and lower abdomen showing hernia overlapping symphysis and dense adhesion of intestine to posterior wall of bladder. Arrow points to vesicle end of vesicovaginal fistula.

Fig. 3.—Bladder laid open exposing urethra, ureters, and vesicle end of vesicovaginal fistula.

1½ inches above and to the left of the right ureter. Attempts to dilate the vagina and soften the scar by means of colpeurysis, applied daily for a period of two weeks, proved unsuccessful.

Under general anesthesia the lower portion of the abdominal scar was excised, the peritoneal cavity being accidentally opened. Exploration showed dense adhesions of the small intestine to the peritoneum covering the posterior bladder wall. The peritoneal opening was securely sutured.

The vagina was then distended with a colpeurynter, the bladder was filled with water through a catheter passed through the urethra, and with great difficulty the apex of the bladder was approached through the space of Retzius. The anterior and lateral walls of the bladder were finally mobilized. The fundus was made accessible but the posterior wall could not be liberated. Access to the vesical cavity was obtained by a T-shaped incision including the fundus and lateral walls, the long arm of the "T" running down anteriorly nearly to the urethra. (Figs. 1 and 2.)

The vaginal colpeurynter was now emptied and withdrawn and a heavy silk ligature, to the vaginal end of which a gauze sponge had been attached, was pulled through the fistulous opening. By suprapubic traction exerted on the silk the deeply situated fistula was thus made more accessible. (Fig. 3.)

The vesical mucosa was now readily liberated around the margin of the fistula. Freshening of that portion of the tract which ran through the vesico-vaginal septum, however, was impossible. Three chromic sutures were passed and tied subvesically in this septum and then three finer sutures were used to unite the bladder mucosa. The bladder was reconstructed with two layers of suture, a catheter being sewed into the fundus by the Kader technic. Ample perivesical drainage was instituted, concluding the long and difficult operation. Convalescence was uneventful. The suprapubic opening closed spontaneously on the eighteenth day after operation.

At the time of discharge, four weeks after operation, a slight amount of urine dribbled from the vagina. Cystoscopy revealed a residual opening 3 millimeters in diameter in the middle of the retracted scar.

Two weeks later the bladder end of the fistula was fulgurated through the cystoscope. Following this treatment the leakage was further diminished, but persisted until two further treatments were given, four months later. Recent cystoscopy (November, 1931) showed a barely visible scar. Continence is now perfect.

If intravesical fulguration had failed in this case, I know of no other method of approach which could have been used.

In the last three years, three rectovaginal fistulae of small size, remaining after otherwise successful repair of deep complete tears of the perineum, have been closed by means of monopolar cauterization. The vaginal opening of the rectovaginal fistula is exposed, a sparking treatment is given around the circumference of the mucosa, the tract itself rarely requiring cauterization. These treatments are very light, an interval of two weeks being allowed to elapse between each. Little more than superficial destruction of the epithelium is attempted, the underlying tissues contracting in a slightly funnel-shaped fashion between treatments until eventually the very thin rectovaginal septum is thickened in this area and completely closed. Another case due to perforation of the septum by a chair rung, also has been treated and closed. In addition, two rectovaginal fistulae situated within one inch of the

fourchette, resulting from suppurative processes secondary to colitis and proctitis, are being subjected to the same treatment. Whether these likewise can be cured is still undetermined, although the suppuration was readily controlled and the tracts are beginning to shrink.

It seems warranted to call attention to and recommend these extremely simple procedures for the closure of both bladder and rectal fistulae. No harm can result if due care is taken not to cauterize to a degree which involves any loss of substance. The procedure merely removes the epithelium, and favors contraction and scar formation.

#### ADDENDUM

Since handing in this manuscript, two additional cases of vesicovaginal fistulae have been observed. The first, C. M., 35 years of age, sustained her fistula during an embryotomy performed 3 years ago. Since then she was operated upon once at another institution. The bladder capacity was *nil* and required gradual dilatation by means of an intra-vesical balloon before cystoscopy could be resorted to. Two small fistulae situated in a trabeculated area between the ureters were closed by two fulgurations.

The second case, R. L., 38 years of age, a para iv, sustained the injury during a delivery ending in stillbirth 6 years ago. No operative intervention had been attempted. The fistula could not be visualized per vaginam, but above the inter-ureteric ridge a 4 mm. opening was seen through the cystoscope. Six fulgurations during the period from May, 1931, to June, 1932, have been given. The fistula is now minute, the leakage minimal, but additional treatments are required to completely close the tract.

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**Aschner: An Especially Effective Method for Conservative Treatment of Inflammatory Adnexal Tumors.** München. med. Wehnschr. 33: 1379, 1929.

Aschner claims that the following method of treatment is extremely effective in pelvic inflammatory disease, whether of gonorrheal or puerperal origin: First, from 5 to 10 leeches are applied to the lower part of the anterior abdominal wall. Second, calomel is given two or three times daily in .01 to .02 gram doses. Third, vaginal suppositories containing ichthyol and antipyrin are inserted, once daily. In cases tending to abscess formation, vaginal globules, containing certain gums (Galbani, Myrrh, Olibani) are used. With this treatment Aschner claims to have avoided many operations. Where surgery was unavoidable, only conservative operation, such as vaginal incision, resection of a tube, or removal of the adnexa on one side, was necessary. Hysterectomy for inflammatory disease was not required in any case under this régime. At least one ovary and a uterus, capable of menstruating, was left in every case operated upon.

A. SHULMAN.

# REPORT OF AN ADDITIONAL CASE OF PUERPERAL SEPTICEMIA DUE TO INFECTION BY CLOSTRIDIUM WELCHII\*

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FOUR years ago, in conjunction with Dr. I. D. Michelson, I reported a case of puerperal gas bacillus infection, with an extended review of previous publications on the same subject. I wish now to present another case occurring in my service, and to examine the literature which has appeared since my earlier paper was published. As the ground was quite thoroughly covered in the earlier paper, it will be necessary at this time only to summarize very briefly the history of this complication of the puerperium, as those interested can refer to that paper and the authors listed in the bibliography attached to it.

A colored woman, aged thirty-eight years, was seen in the seventh month of her eleventh pregnancy. She had had two miscarriages and eight full-term deliveries with easy labors. Seven children were living. Four years previously the patient had received intravenous injections following a four-plus Wassermann reaction. The reaction at present was negative. She was admitted to the Maternity Division of the Memphis General Hospital, June 8, 1931, at 10 P.M., labor having begun two hours before. There were no symptoms of impending puerperal infection other than a mild edema of the extremities, although the membranes had ruptured two days previously. The cervix was completely dilated at 12:30 A.M., June 9, two and a half hours after entrance, and a normal living female infant was spontaneously delivered thirty minutes later, vertex presentation, R. O. A.

As the placenta failed to separate and bleeding was negligible, ten hours were permitted to elapse before manual delivery of the secundines was undertaken. The uterus was then evacuated and packed with mercurochrome gauze. By mistake this gauze packing was permitted to remain in position for twenty-seven hours. When it was finally removed, the patient went into shock. At this time the temperature was normal; the red blood cells numbered 3,500,000; hemoglobin was 70 per cent; catheterized urine was clear and showed neither albumin nor sugar, with an occasional pus cell and two or three blood cells to the high power field. Four hours after removal of the packing, 500 c.c. of 20 per cent glucose solution was administered, following which the patient again went into shock.

On June 11 there was a chill with rise of temperature to 104° F.; the lochia became foul and acute tenderness developed over the uterus. A blood culture taken at this time was negative after five days' growth. The same day antistreptococcus serum was administered, and at 2:30 P.M. the following day 200 c.c. of citrated blood was transfused, with an immediate favorable reaction. At 9 P.M., however, the patient again collapsed and was revived with difficulty. From this time on all the evidences of a fulminating infection were presented, temperature elevation to 103-104° F., foul lochia, acute tenderness on palpation over the uterus, punctuated by periods of circulatory collapse. There was a loss of two million blood cells within two days' time, and a peculiar lemon tint to the skin was observable. Death occurred on the fourth day following delivery.

\*Read at the Third Annual Meeting of The Central Association of Obstetricians and Gynecologists, Chicago, Illinois, October 29-31, 1931.

*Pathological Report.*—The specimen consisted of a parturient uterus amputated supravaginally. The walls of the cavity were very foul-smelling, black, and necrotic. The myometrium was unusually friable and thick, presenting the appearance of a sponge filled with gas. Hemorrhagic and hemolytic areas were visible in all parts of the uterus, rendering the entire specimen dark-brown in color. Microscopically, the cavity lining consisted principally of fibrin, hemolyzed red cells, necrotic tissue, and bacteria. No staining was present in the nuclei of the muscle cells and thrombosis of the blood vessels was marked. The tissues were infiltrated by polymorphonuclear cells, while large gas pockets lined by clouds of blue-staining bacilli were in evidence throughout.

*Diagnosis.*—Acute puerperal endometritis and myometritis: Invading organism, *Clostridium welchii*.



Fig. 1.—Acute puerperal endometritis and myometritis due to *Clostridium welchii*. Sagittal section of the soft, flabby, and enlarged uterus. Cavity is lined with ragged greenish-black, decomposing tissue and the myometrium shows many gas spaces.

At the time of publication of my previous case we were able to find 41 reports of puerperal infection due to the *Clostridium welchii* which had previously appeared in literature. To these 42 I wish to add the one just recorded, and 13 gathered from the literature published since the presentation of my previous paper. These are: The case of Beare and Cleland of the University of Adelaide, Australia (1927); the two cases reported by Cleland in conjunction with Margarey and Sleeman in the same year; one case by Kamniker, one by Guggisberg and one by Pfalz, all published in German during 1927; one case by Ivens of Liverpool, and six cases from St. Thomas' Hospital, London, described to the Royal Society of Medicine by A. J. Wrigley. I found no new reports in American periodicals.

The conclusions drawn from our previous study were as follows:

1. A summary of the recorded cases shows that abortion is the most important cause in the etiology of gas bacillus infection.

2. Pain in the abdomen, fever, rapid pulse, jaundice, cyanosis, air hunger, hemoglobinuria, rapidly progressive secondary anemia with pathologic bone marrow cells in the circulating blood, form the clinical entity for the diagnosis of gas bacillus sepsis.

3. Hysterectomy, administration of antitoxin, and blood transfusion seem to be the most logical methods of treatment.

Examination of the recent literature does not lead to any marked change in the conclusions previously drawn. Several of the British and



Fig. 2.—Section through endometrium of fundus of uterus showing masses of fibrin, cell debris, and clumps of bacilli. To the right is necrotic, smooth muscle of myometrium. ( $\times 96$ .)

German writers have gone very extensively into the possibilities of puerperal infection by pathogenic anaerobic bacteria, but the sum total of their findings does not materially enhance the knowledge which we already possessed. The findings of the Australians are, however, of particular interest. They tell us: "It would seem that in Adelaide during recent years there have been an undue number of infections of the uterus with anaerobic gas-forming organisms. The patients have all aborted at an early period of pregnancy, from the second to the fifth month. All have denied interference but we have thought in all instances that such interference had probably taken place, although there was no evidence of it. It has seemed to us that the most likely explanation of how the gas-forming bacteria had reached the interior of the uterus was by the introduction of fecal specks at the end of some implement used for bringing about abortion. The vulval hairs and orifice must frequently be contaminated with bacteria of fecal origin. The passage of an instrument, unless in expert hands and after thorough cleansing,



must surely be likely from time to time to carry fecal material containing organisms into the interior of the uterus. Once lodged there and the abortion commencing, the anaerobic organisms might find, in blood clot and necrotic material in the uterine cavity, an excellent nidus for their development. Considerable multiplication could here occur leading to some surrounding necrosis of injured tissue. The clots occurring in the uterine veins are probably later invaded."

In my previous review it was found that criminal abortion comprises 60.97 per cent of the cases of *Clostridium welchii* infections, thus agreeing with the findings in Adelaide. However, until more accurate labora-

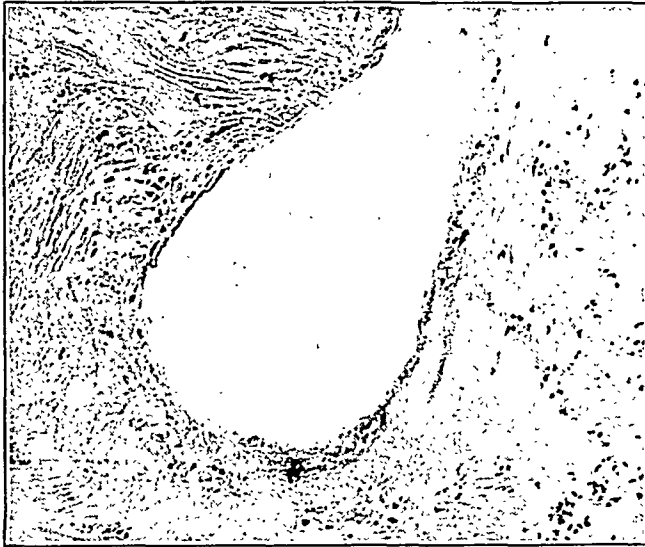


Fig. 3.—Section through myometrium of fundus of uterus showing a gas space partly surrounded by bacilli. To the right the necrotic, smooth muscle is infiltrated with polymorphonuclear leucocytes. ( $\times 96$ .)

tory work is done, the exact means whereby the organism is introduced into the uterus must remain an open question. Schottmüller claims that the organism may occasionally be found in the vagina of normal healthy women and that autoinfection is possible. Most investigators deny this possibility. It is well known that the organism is widely distributed in nature and occurs normally in fecal contents, so that a ready source of the organisms is always present. Instruments used in abortions unless sterilized and introduced aseptically would furnish the most common method whereby the organisms are conveyed into the uterus. Cultures from the vulval hairs and orifice for the presence of members of the gas gangrene group should be done before they can be incriminated as the focal habitat of this group of organisms.

The clinical picture given by all the authors is strikingly similar to that we ourselves observed. The jaundice is especially stressed. One author remarks that there would seem to be reason to believe that many cases of "acute yellow atrophy of the liver" appearing as a complication

of the puerperium, were actually due to gas bacillus infection which was not recognized.

The most extended investigation of the mode of infection is that of Wrigley. I agree with Wrigley that dead tissue must be present before *Clostridium welchii* can implant itself and propagate in sufficient numbers to initiate puerperal infection. This was emphasized in my previous review of this subject, showing that criminal abortion and operative procedure are most likely to result in the production of this type of puerperal sepsis since they serve as a ready means of introducing the organisms and at the same time are likely to produce death of the tissues. However, death of the fetus is not a necessary requirement for this condition to occur. This is readily seen in the case just reported where a live fetus was delivered. Furthermore, if the infection remains limited to the fetus or to the endometrium, the symptoms may be slight and the patient usually recovers even though the organism is found in the blood stream. It is, however, when the organisms gain entrance into the uterine musculature that the condition becomes serious, producing one of the following three conditions: (a) physometra, (b) emphysema of the uterine walls, and (c) gas sepsis. It is still an open question whether the trauma incident to normal physiologic labor with its anaerobiosis due to blood clots is not sufficient background for the development of gas gangrene, provided organisms are introduced from without.

In résumé, the following conditions should make one suspect the possibility of puerperal gas gangrene sepsis: (1) trauma to the uterus induced either by abortion or prolonged labor with its incident operative procedures; (2) clinical symptoms of infection evidenced by fever, rapid pulse, pain over the uterus, and foul discharge; (3) signs of rapid red blood cell destruction, manifested by a very severe anemia, almost fulminating in its development, and by jaundice. The *Clostridium welchii* elaborates two types of exotoxins, namely, a myotoxin causing death of muscle and a hemotoxin causing hemolysis of the red blood cells. Puerperal gas gangrene is unique in that most of the signs are due to the hemotoxin and the myotoxin effects are rather in abeyance as contrasted with the ordinary traumatic gas gangrene in which the myotoxin produces most of the damage and signs. It is to be emphasized that one should not wait for the development of signs of gas, i. e., crepitation, before diagnosis of puerperal gas gangrene is made. Crepitation is elicited only in a very small percentage of cases during life in this condition.

*Treatment.*—Wrigley's deductions are of special interest in relation to treatment, a phase of the subject with which he deals in some detail. Heretofore, treatment has taken up but little space in the article devoted to the subject of puerperal gas bacillus infection, for the very excellent reason that the condition is so fulminating that time to institute treatment is usually lacking. Some of the patients died within four hours of the recognition of the presence of the gas bacillus.

It is the assumption of the Australian investigators that all instances of puerperal gas bacillus infection are related to abortions, usually self-induced. Wrigley argues from the premise of intrauterine death of the fetus, which may occur at term, or prematurely from causes other than outside interference. In neither of my cases did these premises have place. In the case first reported, labor was at term, but delivery was impeded by the presence of uterine myomas. A midwife had made repeated vaginal examinations, however, which would provide the first condition set forth by Wrigley, and the long-contained exhausting labor would provide the second.

In the case which is the subject of the present paper, delivery was premature, and the membranes had ruptured two days before entrance into the hospital. Vaginal examination carried out in the interval would provide a possible means of entrance for the organism, if it were present upon the labia or elsewhere about the vulva, as the Australian writers have suggested. The error in permitting the packing to remain so long in the uterine cavity would supply the circumstances required to fill Wrigley's second condition.

It is evident that treatment to be effective must be initiated *before* the presence of the gas bacillus is made evident, in other words before the diagnosis is made. It would, of course, be out of the question to administer prophylactic serum, for example, to every parturient woman. But given the special circumstances which have just been outlined, the institution of prophylactic treatment along the same general lines as are now followed in the prevention of tetanus, might very well prove valuable. Frances Ivens relates her experience with the administration of Weinberg's anti-gas-gangrene serum, given subcutaneously at the time of the removal of the dead fetus, while the mother was still under the anesthetic. The patient made complete recovery. The diagnosis was made on the "gangrenous odor" before crepitation or other signs of gas infection had supervened.

The use of serum is, of course, still in the experimental stage, but its use would seem quite as logical as the other methods which are advocated; that is, hysterectomy and blood transfusion. To be effective the anti-toxin must be administered before the infection becomes fulminating, and all too often, no thought of this type of infection is taken until the damage has gone beyond repair. The condition is too rare to permit its being readily recognized, even by obstetricians of long experience. It is desirable that more attention should be given to it, however, as it may well be more common than we at present realize. The careful reporting of every case observed, and continued experiment as to the best means of prophylaxis treatment, is essential for the control and eradication of this serious hazard to maternity.

I am indebted for the illustrations of this paper to Mr. Joseph L. Scianni, artist of the University of Tennessee Pathological Institute.

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889 MADISON AVENUE.

## POSTOPERATIVE SEPARATION OF THE CESAREAN SECTION WOUND, WITH SUBSEQUENT ABDOMINAL PREGNANCY. REPORT OF FOUR CASES\*

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**R**UPTURE of the cesarean section scar during labor is not at all uncommon. It usually occurs during the first labor after the section, but cases are on record in which this particular labor was terminated successfully by vaginal delivery, only to have rupture of the scar in the next labor. Rupture before labor has begun is also by no means infrequent. It is generally held that the cicatrix following the classical operation is more likely to give way than the one due to the low section. This is denied by some, who hold that statistics will ultimately show a much higher incidence of rupture of the low section scar than is at present admitted by those advocating this operation.

In rupture of the scar of the classical section immediate laparotomy offers the only chance of saving the mother (the child is practically always lost), and even this is often of no avail, as the hemorrhage is so rapid and so profuse that death supervenes rapidly. On the other hand, rupture in the relatively avascular lower segment is not associated with such free bleeding, unless the uterine vessels are involved, and hence the prognosis is much more favorable.

The cases under discussion in this report, however, can hardly be classed as instances of rupture of the scar, but would rather fall under the heading "postoperative separation of the cesarean section wound." So far as I know, such a condition has not heretofore been reported. A brief review of these cases will be of interest.

**CASE 1.**—The patient was a young white woman, admitted to my obstetric service at the Charity Hospital, with a history of a classical section for eclampsia two years previously; as far as she could judge, the convalescence had been uneventful. She complained of indefinite abdominal pain, which had developed about two days

\*Read at a meeting of the New Orleans Gynecological and Obstetrical Society, November 12, 1931.

previously. Up to that time, the pregnancy had progressed normally, with no history of pain, bleeding, or other untoward development. Examination showed her to be somewhat emaciated and underweight, but otherwise in fair condition and not acutely ill. She was not confined to bed while the preliminary studies were being made. On abdominal palpation the fetus was found to be lying rather high, and obliquely placed, but not in a definite transverse position. There were no heart tones or other evidence of fetal life. Skiagraph confirmed the diagnosis of death of the fetus, the cranial bones being somewhat overlapped. Spontaneous labor did not develop (naturally enough, as will be seen later), hence induction of labor was apparently indicated. Up to this time, of course, the only diagnosis considered was that of intrauterine dead fetus. The possibility of rupture of the scar a few days prior to admission was taken into account, but the idea was dismissed because of the mild character of the symptoms and the condition of the patient.

A rubber catheter, of fair size, was easily passed into the cervix without anesthesia, the whole catheter being inserted, and a light cervicovaginal pack was employed to retain it in place. There were no developments. The pack was removed at the end of twenty-four hours. Four days after insertion of the catheter, an attempt was made to remove it, but its tip could not be located. A bag was then placed in the cervix, without avail, and it was removed at the end of thirty-six hours. Seven days after insertion of the catheter, signs of peritoneal irritation developed, and then it began to dawn upon me that I must be dealing with a case of rupture of the scar, which I thought must have occurred shortly before admission, in spite of the mildness of the symptoms. Dr. Alton Ochsner agreed that laparotomy was indicated.

*Operation.*—The abdomen was opened in the midline, and the intact amniotic sac was found just beneath the peritoneum. This was opened, and a dead, somewhat macerated fetus was removed. The catheter was lying free in the abdominal cavity, outside the membranes, and was also removed. It was now found that the placenta was adherent to the anterior surface of the omentum, which in turn was adherent to the fundus of the uterus. The attachment of the placenta was extensive and firm, but, as is usual in such cases when the fetus has been dead for some time, it was easily separated. It was now found that the cesarean section incision in the uterus was open for its entire extent, but it could be seen that the separation of its lips was not a recent affair, as they were covered with well organized exudate, and the omentum was adherent to their outer margins. As the general condition of the patient was very poor, no attempt was made to repair or remove the uterus, and the abdomen was closed, with a drain in the lower angle, down to the uterus. The patient was very ill for several days, but she eventually made a complete recovery. She was advised to return for another operation.

Three months later she returned and was admitted to the gynecologic service of Dr. C. Jeff Miller. She was in excellent health. Laparotomy by Dr. Miller revealed an abdominal cavity free from adhesions, except that the thoroughly involuted uterus was still adherent to the omentum; the section wound was still open. He did not think it advisable to attempt to repair the uterus, hence a supravaginal hysterectomy was performed. Convalescence was uneventful.

CASE 2.—This was a colored woman who had had two previous sections for contracted pelvis, the second, an elective one, having been performed in the Charity Hospital, two years previous to the present admission. Review of this record showed that the operation was of the classical type, catgut being used as the suture material. The convalescence was uncomplicated and afebrile. She was admitted in her third pregnancy about two weeks ahead of the estimated date of delivery. Examination revealed a healthy, rather underweight negress with a generally contracted pelvis. The abdominal wall was very relaxed, and the fetus and its parts could be easily palpated. This fact aroused no suspicion, due to the thinness and relaxation, anal-

ogous to the condition so often found in multiparae. The fetus was alive on admission. A third section with sterilization was advised and accepted by the patient. Examination one week after admission disclosed the fact that the fetus was dead, but it was deemed best to carry out the proposed operation.

The abdomen was opened, and I was greatly surprised to find the membranes immediately under the peritoneum. The sac was opened and the dead full-time fetus was removed. Again the placenta was found to be adherent to the omentum, this time to the posterior surface. It was attached over a wide area, but was easily removed without hemorrhage. The omentum was adherent to the uterus laterally and to the edges of the wide open cesarean section wound. This incision presented no evidence of recent rupture, but it had evidently been open for a long time, as the surface of the incision was covered with organized exudate, as in the first case. The patient was in excellent condition, so a supravaginal hysterectomy was performed. Recovery was uneventful.

CASE 3.—This patient was a young negress, whose first pregnancy had been terminated by classical section for eclampsia two years previously in another city. She was admitted to Charity Hospital a few days previous to the expected date of delivery, with a history of absence of fetal movement for two weeks. She presented evidences of a mild toxemia; poor appetite, malaise, a pulse of 100, but no fever. (I have noted that these toxic symptoms are much more frequent in cases of abdominal pregnancy with dead fetus than in intrauterine fetal death.) The fetus was lying transversely above the umbilicus, the head to the right. No fetal heart tones were heard. The position was confirmed by a skiagraph, which also showed marked overlapping of the bones of the cranial vault. A hard, rounded mass was felt between the fetal body and the symphysis pubis; it was concluded that this was the uterine body. Lipiodol injection was done, and the skiagraph showed the lipiodol in the lateral aspect of the pelvis below the fetal body. In view of our experience with the first two patients, we felt that we were dealing with the same condition.

*Operation.*—The abdomen was opened below the umbilicus, through the cicatrix of the previous section. The placenta was encountered, and was found to be attached to the parietal peritoneum along the previous incision, and to the upper portion of the uterus. A thick broad band of omentum was found, anterior to the membranes and attached below to the uterus. The placenta, membranes, and fetus were removed. It was found that the fetus had been lying between the intestines above and the uterus below. The uterus was adherent to the rectum posteriorly and to the abdominal wall anteriorly, as well as to the omentum and the placenta. The bladder could hardly be identified, because of the adhesions. The adhesions were freed, and approximately half of the uterus was removed, to a point just below the old section incision. It was felt that an attempt at a more complete removal of the organ might result in an injury to the bladder. The tubes and ovaries were not removed. After the peritoneal toilet, the abdominal wall was closed in layers without drainage, the closure being reinforced by through and through silkworm sutures, as postoperative wound separation was feared, because of the friability of the peritoneum at the side of the placental attachment. The patient made an uneventful recovery, her condition being much improved by a blood transfusion, later in the day of the operation, not urgently indicated, but thought to be advisable.

CASE 4.—Another case of this character was operated upon in Charity Hospital by Dr. Roy Wright about one year ago. Abdominal pregnancy was diagnosed and separation of the cesarean scar was suspected. At operation the placenta was found to be attached to the edges of the uterine incision (which was wide open as in the three cases reported above), and to the omentum and to coils of the small intestine. The fetus, placenta, and membranes were removed, and supravaginal hysterectomy was performed. The patient died on the fourteenth day from ileus.

## COMMENT

I feel that in each of these patients the course of events was as follows: The catgut was absorbed rather rapidly during the convalescence from the operation, as is sometimes the case in the abdominal wall, and the uterine wall consequently gaped open. As all the previous operations were elective sections there was no infection, hence only organisms of a low degree of virulence were in the uterine cavities, and their escape merely caused omental adhesions, rather than general peritonitis. I may say here that in another patient operated upon in the hospital some years ago, peritonitis developed eight or nine days after cesarean section; the recovery up to that point had been complicated by a febrile reaction. At autopsy the cesarean wound was found to be wide open, and streptococci were found in the uterine and abdominal cavities. To resume: in each of the cases reported, granted that the ovum was fertilized in the tube, it evidently pursued its usual course and reached the uterine mucosa. If it imbedded itself at all, the implantation must have been transient. It is more reasonable to conjecture that, as the uterine cavity was wide open, with no anterior wall, and with the omentum adherent to the edges of the open incision, the fertilized ovum simply traveled on up and attached itself primarily to the omentum in three cases and to the abdominal wall in the other. Thus, in each instance, I believe that the abdominal pregnancy was primary. Certainly the broad and rather firm placental attachment found in each case was not of recent development, hence I feel sure that the implantation did not follow a rupture of the wound in the latter part of pregnancy. Nor is it reasonable to suppose that a healed wound (even though poorly healed) would open up early in pregnancy, with subsequent secondary abdominal pregnancy.

It is rather remarkable that four such cases should be encountered in one hospital in the space of two years. Certainly unreported instances of this condition must have been encountered elsewhere. The possibility of this development should be borne in mind when classical section is contemplated. In my opinion, we are taught three lessons by the study of these patients. First, that we should be very sure that cesarean section is the only solution of the problem presented in a given case (and this rules out practically all cases of eclampsia). Second, that the uterine incision must be very carefully sutured. Third, that additional evidence is presented demonstrating the superiority of the low segment section (laparotrachelotomy).

# LACERATION OF FEMALE URETHRA WITH COMPLETE INCONTINENCE, METHOD OF REPAIR RESTORING FUNCTION

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THE patient, E. W., No. 44227, aged twenty-nine years, had complete incontinence. (One baby was born four years ago, who died at nine months from pneumonia.) She was admitted to the obstetrical ward of another hospital, was eighteen hours in difficult labor and had severe lacerations. The urethra (Fig. 1) had been lacerated in a transverse direction through its axis from the external os into

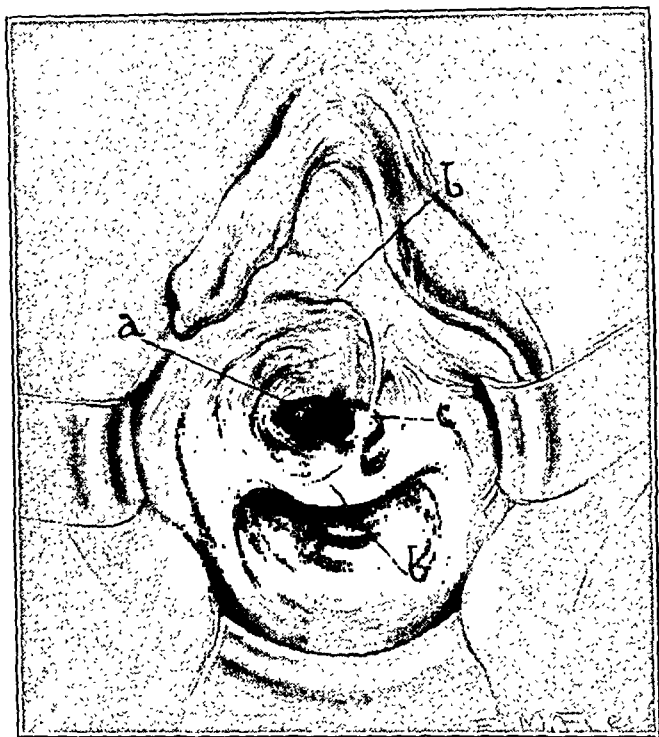


Fig. 1.

the posterior sphincter of the urethra leaving only a few fibers of the sphincter intact. One could look directly into the bladder. The free flap, hinged posteriorly, was lightly held in position by a small strand of mucosa about 2 mm. in diameter joining the original external orifice to the free end of the flap.

Note on discharge: Vaginal wall firm, ulcerated. No further pregnancies. Able to control urine until two weeks ago when function became involuntary. The urine ran from her constantly, keeping the bladder empty.

The problem presented was to restore the sphincter function, using the combined bladder and urethral muscles, and to restore the urethra. It was believed that the fibers in the flap would still function if properly united to their fellows. A two-stage operation was therefore decided upon to allow the flap to develop its blood

\*Read before the New York Academy of Medicine, November 24, 1931.



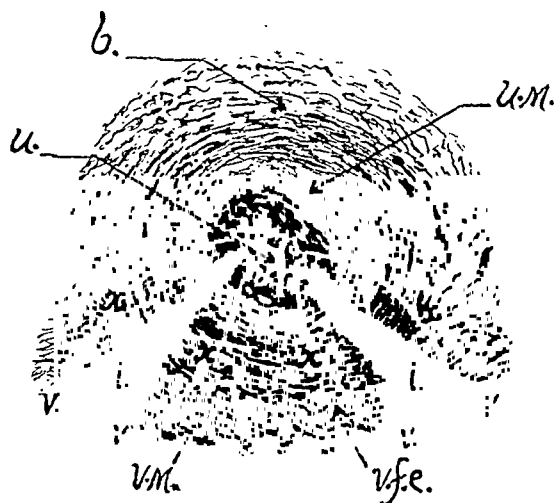


Fig. 2.—Transverse section of urethra through which injury took place. *t*, urethral injury—bilateral; *x*, lines of excision for reconstruction; *u*, urethral canal; *u.m.*, muscular coat of urethra; *b*, bladder wall; *v*, vaginal mucosa; *v.m.*, muscular coat of vagina; *v.f.e.*, fibroelastic coat of vagina.

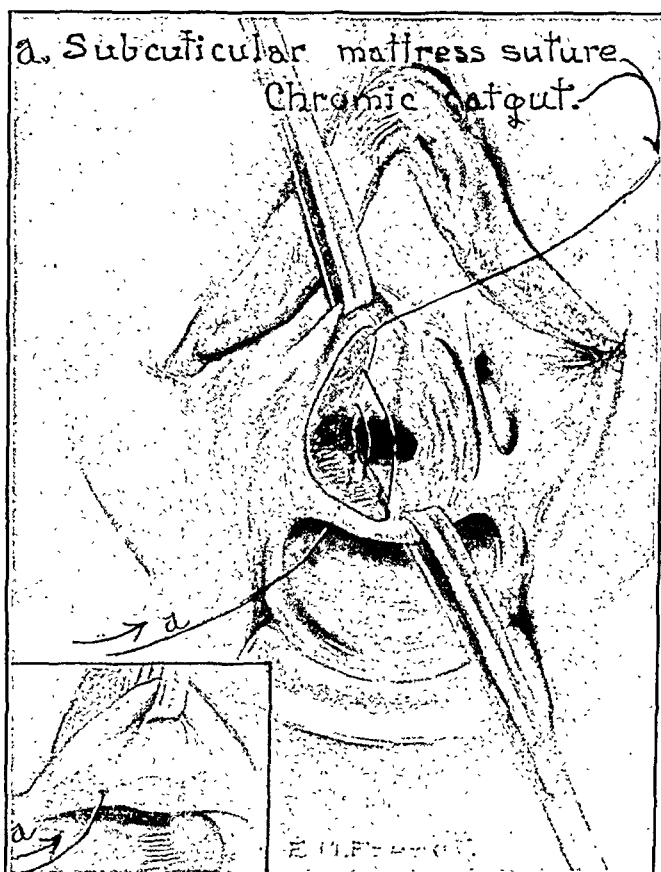


Fig. 3.

supply from one side before the other was sutured. Fig. 2 illustrates the tissues through which the injury occurred and the lines of denudation are graphically shown.

Minimum trauma by dissection and passing of sutures was planned. A method of inserting silver wire sutures through a shaped Vim rustless steel hypodermic needle (for which the author makes no claim of originality) was used. Denudation by sharp dissection was done following the margin of the urethral mucosa and extending well down into the musculature of the bladder. (Fig. 3.)

A number one chromic catgut suture was passed from the vagina into the median angle of the denuded area and this suture was continued along the urethral margin as a submucous mattress suture to the external os. At this stage the silver wires

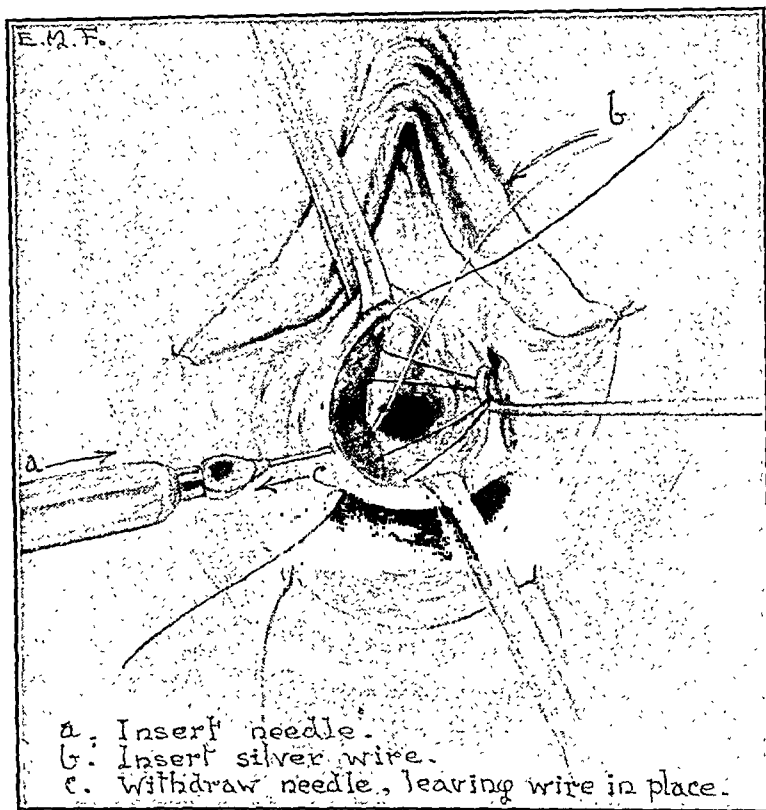


Fig. 4.

were passed through the shaped Vim rustless steel needles as illustrated in Figs. 4 and 5. The chromic suture was again continued down the lateral margin of the denuded area as a submucous mattress suture; and when the angle was reached, it was passed through into the vagina, pulled tightly, and tied. The margin of the denuded area was thus neatly approximated and there was absolutely no bleeding. The four silver wires were then loosely twisted, the ends threaded on a perforated lead shot, and placed in the vagina. (Fig. 6.) Thus, the closure was effected by four silver wires and one chromic catgut suture.

Following the first stage of the operation which was done August 27, 1929, a straight retention catheter was inserted at operation and soon removed. Primary union occurred and the silver wire sutures were removed on the fourteenth day after operation. The second operation was done on September 17, 1929; the left side was repaired similarly to the right. A straight retention catheter was inserted and remained in two and three-fourths days. From then on the bed was dry and no further

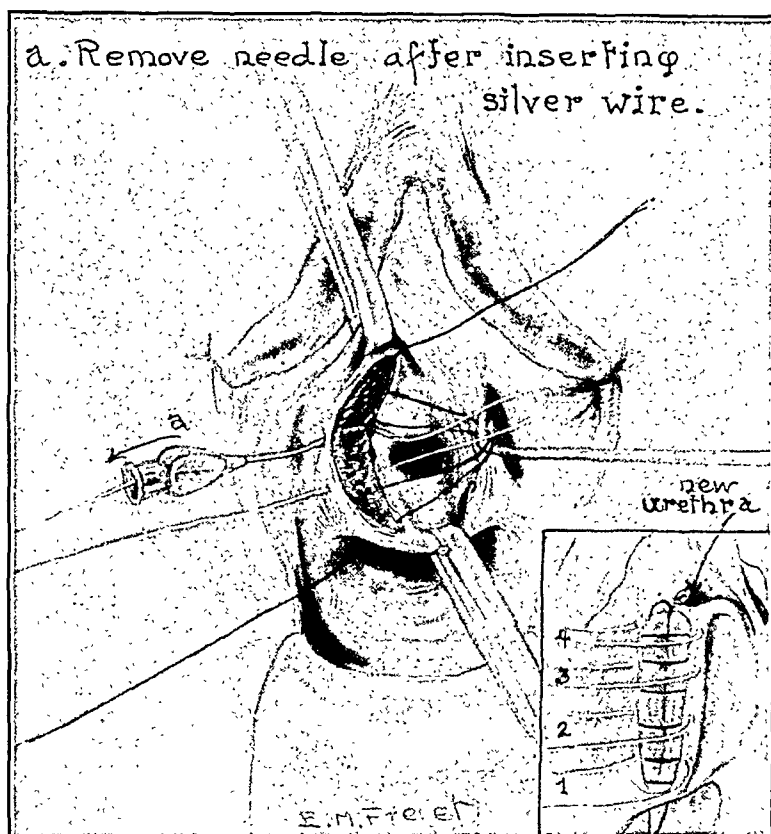


Fig. 5.

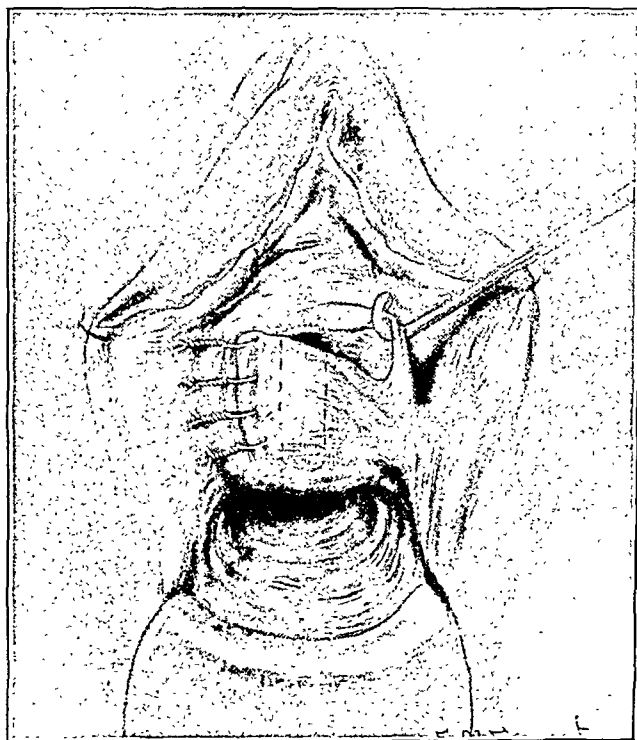


Fig. 6.

catheterization was necessary; the patient was able to retain from four to fifteen ounces before voiding. Sutures were removed on the fourteenth day after operation and she was discharged three days later with complete control of urine. (Fig. 7.)

*Follow-up.*—November 13, 1929: Patient in excellent health, no symptoms. Has full control of urine. Urethra well healed, very little scar tissue, normal urethral orifice.

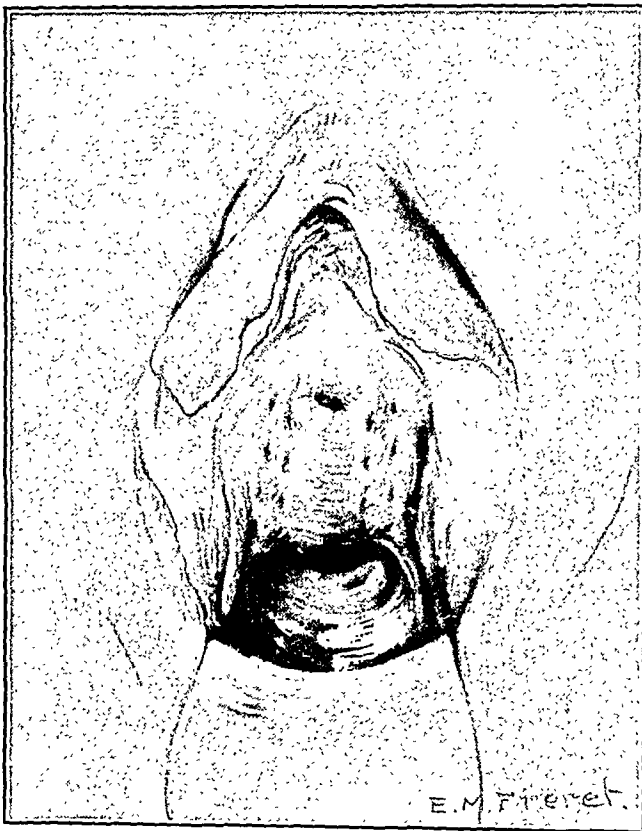


Fig. 7.

February 25, 1931: Patient states she is able to control her urine except when she gets a cold and is obliged to go to the toilet in a hurry. Examination shows a good urethra with an apparent satisfactory sphincter control.

The author wishes to thank Dr. George Gray Ward for the privilege of carrying out this method of treatment and for his interest in the result.

163 EAST SIXTY-FIRST STREET.

# FULL-TERM PREGNANCY IN UTERUS BICORNIS, WITH ANTERIOR SACCULATION OF THE PREGNANT HORN

EULA ENO, M.D., SHANGHAI, CHINA

THE patient was admitted to the Obstetrical Service of the Margaret Williamson Hospital on March 16, 1930. She was thirty-one years of age, and in her second pregnancy. Her first had been uneventful, the labor spontaneous, at term, and the child born alive. The child had died at the age of four, of some acute illness.

The second pregnancy was uneventful. Labor had set in ten hours before admission, and the pains had increased in severity and frequency in a seemingly normal way. The patient was extremely uncomfortable on admission because of distention of the bladder. She stated that she had passed no urine for forty-eight hours. She had been examined by a midwife, who had advised that she seek help at a hospital. Fetal movement ceased four hours before admission.

Entrance examination revealed nothing of moment in the general condition of the patient, pulse 90, temperature normal, blood pressure 130/90, and her general appearance not that of an acutely ill person. Abdominal examination was striking. The whole of the right side of the lower abdomen from the brim of the pelvis to just above the umbilicus was filled by a rounded tumor mass, fluctuant, obviously the distended bladder. Its outline was very distinct. Just as distinctly outlined on the left side of the abdomen was a second tumor, extending from the brim of the pelvis to a point three fingerbreadths below the level of the xyphoid. This was evidently the uterus. Palpation of the abdomen did not disclose any tetanic contractions of the uterus, and the fetal parts could be mapped out easily. The head occupied the upper pole, and the back was felt anteriorly. The presenting part at the inlet was not made out, because of the distention of the bladder. No fetal heart sounds were heard.

At the vulvar orifice there was a protruding mass, round, pinkish in color, covered by mucous membrane, thought to be either a fold of relaxed anterior vaginal wall, or an unusually large cystocele. Both explanations were proved untrue, when an attempt was made to catheterize the patient. The urethral opening had been pushed high up, so that it lay practically behind the symphysis pubis. Great difficulty was experienced in finding a rubber catheter stiff enough so that it would enter the bladder, but when one was finally inserted, there was evidence neither of excessive lengthening of the urethra and bladder neck, nor of any communication of the bladder proper with the mass at the vaginal orifice. Seventy ounces of urine were obtained and the patient experienced great relief.

It was during the process of catheterization that the true nature of the vaginal mass was discovered. For it was found that there was a tiny opening on about the midpoint of the tumor, through which meconium could be extruded by pressure above or below. Rectal examination had given no satisfaction concerning the cervix, its location, or the amount of dilatation. Vaginal examination now confirmed the uterine character of the vaginal mass. The cervix was pulled high and to the patient's right in such a way that its opening lay on the right posterior aspect of the intravaginal tumor. The dilatation was about 3 cm., and the canal was only partially obliterated. The presenting part of the fetus was easily distinguished as a breech, which was not only engaged, but had in reality already passed the outlet of

the pelvis, although it was still contained with the uterine cavity. A diagnosis of anterior sacculation of the uterus was made, and a Porro-cesarean section advised.

The abdominal incision was kept well to the left of the midline, because the uterus had retained its position in the left half of the abdomen, even after the bladder had been emptied. There was nothing unusual about the cesarean proper, save the fact that the fetus had descended so far into the pelvic canal that it was hard to dislodge from above. Traction on the feet was of no avail, so a hand was used as a lever under the head, and after the head and shoulders had been delivered the body followed easily. As soon as preparation was made to deliver the body of the uterus in order to proceed with the supravaginal hysterectomy; it was discovered that the uterus was bicornuate, deeply bifurcated. The right horn lay on the floor of the pelvis, a spindle-shaped structure, about 12 cm. in length, and 5 cm. in diameter at its greatest circumference. The whole of this horn, and the tube and ovary on that side, were easily clamped and freed for amputation at the cervix. Greater difficulty was encountered on the other side, however. The round ligament and the vessels in the broad ligament were ligated as usual, and the broad ligament cut down the side of the uterus in the usual manner. But when attempt was made to pull the body of the uterus up far enough to expose the uterine artery, and the junction of the cervix and body, it was found that the lower uterine segment had so far prolapsed into the vagina that the exposure was not good. The resultant amputation was rather amputation through the lower half of the lower uterine segment, than an entire removal of the body of the uterus through cervical tissue. Hemorrhage was severe, but not alarming, and was easily controlled. The stump, which consisted of cervical tissue through its right half, and of uterine mucous membrane anteriorly and to the left, was closed, and the peritoneum was used to cover the pelvic floor. A cigarette drain was left at the lower angle of the wound, and the abdomen closed.

The postoperative course was uneventful, fever being present for a week, but the temperature never went higher than 102°. There was almost no drainage from the wound, and the entire wound was dry by the sixteenth day. Examination on the twenty-eighth day showed a small cervix somewhat to the right of the vaginal vault. The entire vault and the fornices were clear. The anterior wall of the vagina, especially to the patient's left was redundant and relaxed, and protruded from the vulvar orifice, even with the patient lying down. At the most dependent point of the relaxed pouch of vagina, there was an opening, almost invisible, through which there was a leucorrhœal discharge. This was undoubtedly the opening through which meconium had passed before operation.

One year after operation the patient was brought back for examination, and was found to be in excellent condition. She had no leucorrhœa, nor any local discomfort of any sort. Vaginal examination at this time revealed the cervix very small, very high in the vaginal vault, and more nearly in the center of the vault than on discharge from the hospital. The pouch of vaginal mucous membrane had entirely disappeared, and there was nothing abnormal about the vagina except a possible very slight redundancy of the anterior wall.

Anterior sacculation of the uterus is not a common complication in obstetric patients, and I have been unable to find any discussion of the condition in the literature available to me. There is mention in nearly all textbooks of the possibility of a sacculation as a sequela in cases where operative procedures or inflammatory conditions have led to adhesions between the fundus uteri and the peritoneal lining of the abdominal cavity. Such sacculations are evidently intraabdominal when they occur, however. There is an illustration in Williams' text-

book of a posterior sacculation which has been described by Oldham. And if the relative positions of the cervix and saculation were to be reversed, my case and Oldham's case would be very similar. That is to say, in the case described here the sacculation is such that the cervix pointed posteriorly, and up, while in Oldham's case the cervix was behind the symphysis pubis.

The exact mechanism by which the sacculation may have been caused in this case is a little difficult to determine. The first pregnancy had evidently been in the same horn as was this second one, for the right horn, while not rudimentary in the strict sense of the word, had a definite cervical connection with the larger horn, and had certainly never undergone the hypertrophy of a full-time pregnancy. The question, then, is whether the bicornuate nature of the uterus was a mere coincidence or whether the presence of the right horn was indirectly the cause of the sacculation. Did it so displace the pregnant horn, and the cervix, as to prevent its normal enlargement, when this second pregnancy took place in it? And if the interference was due to the presence of the nonpregnant horn, just how did it cause the sacculation to occur? The strongest evidence of displacement of the pregnant horn as a causative factor in the production of the sacculation seems to me to lie in the fact that the whole fundus lay in the left half of the abdomen at the time of operation as if its displacement had existed for a long time. And that displacement, added to the vaginal relaxation which probably followed the first pregnancy, might certainly bring about the eccentric prolapse of the lower uterine segment, which eventually resulted in the sacculation.

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**Nahmmacher:** *The Theory and Practice of Intra-uterine Charcoal Therapy.*  
*Ztschr. f. Geburtsh. u. Gynäk.* 96: 155, 1929.

The author recommends the intrauterine use of charcoal in the following cases:  
(1) In infected abortions either before or after the emptying of the uterus;  
(2) in puerperal endometritis, but not before the seventh day postpartum;  
(3) prophylactically, in cases where a cesarean section had been done after rupture of the membranes.

DR. LESTER E. FRANKENTHAL, JR.

## PREGNANCY IN AN INTERPOSED UTERUS\*

RALPH A. HURD, M.D., F.A.C.S., NEW YORK, N. Y.

*(From the Clinic of the Woman's Hospital)*

THE case is that of a woman in her thirty-fifth year who came to seek relief from symptoms of bearing down, abdominal pain, backache and general asthenia, which were the result of birth injuries. She had been married thirteen years and had had one abortion and three full-term pregnancies. While she was short and weighed nearly 170 pounds, she was, none the less, a healthy vigorous young woman and by both clinical observation and laboratory findings was adjudged a good risk for the surgical undertaking which the lesions she presented would require. The preoperative diagnosis was established as complete movable retroversion of the uterus with beginning slight descensus, cystocele of moderate degree, stellate laceration of the cervix and old laceration of the pelvic floor with relaxed outlet and small rectocele. Operation for repair of these defects was decided upon, including sterilization and carried out twenty-seven days after the last menstruation, including a Watkins interposition operation.

The immediate postoperative course was smooth and uneventful. But about two months after her dismissal from the hospital she again appeared with the complaint that no menstruation had occurred since before her admission, and she was in the throes of vomiting and other subjective signs of early pregnancy. Examination proved that her apprehension was justified and that an intrauterine pregnancy corresponding to the time elapsed since her last menstruation was present. The explanation of this quickly became apparent when it was recalled that there was no curettage performed at the time of operation, she evidently having conceived sometime in the three weeks' period which elapsed between her menstruation and her admission to the hospital.

In view of the abnormal site of the uterine corpus, the amputation of the cervix and the high reconstructed perineal body cesarean section was chosen as the only logical method of delivery. Her pregnancy was for thirty-five weeks uneventful, and it was elected to perform the section at estimated term or immediately at the onset of labor, even if premature. About five weeks from term she began to bleed from the vagina to such an extent that a marginal placenta previa or a low implantation was strongly suspected although not positively verified by physical examination. After twenty-four hours' observation in the hospital the cesarean section was performed under general anesthesia, and a viable infant of five and one-quarter pounds delivered. There was considerable distortion of the pelvic organs consisting of an unusually high, thickened and indurated bladder fold which was intimately adherent to the corpus well up to the fundus and sacculaton and hypertrophy of the posterior wall of the uterine body. As a result of this, the incision into the uterus was on the summit and to some extent on the posterior wall. Operative recovery was uneventful. Involution of the uterus was complete and the patient today is enjoying excellent health. The uterus has again settled down into its place in front of the bladder, and the anatomic result of the plastic work is as satisfactory in every detail as if there had been no intercurrent pregnancy. This case demonstrates the desirability of curettage as an indispensable step in the performance of this type of plastic operation upon a woman in the childbearing period.

37 EAST SIXTY-FOURTH STREET.

\*Read at a meeting of the Obstetric Section of the New York Academy of Medicine, November 24, 1931.



# A CASE OF PUERPERAL INFECTION WITH DELAYED OPERATION\*

NELSON B. SACKETT, M.D., F.A.C.S., NEW YORK, N. Y.

*(From the Clinic of the Woman's Hospital)*

THE following case illustrates a sequence of affections of the genital tract, occurring in a patient confined, and later operated upon, at the Woman's Hospital.

## CASE REPORT

Mrs. B. M., gravida ii, age 32, first came to the Prenatal Clinic on February 18, 1930, when she was found to be thirty weeks pregnant. There were no symptoms and signs pointing to disease of the adnexa. After a pregnancy featured by severe and refractory secondary anemia of unknown cause, she was delivered May 30, 1930, at full term after decomposition of frank breech (L. S. A.) and extraction after a first stage of nineteen and one-half hours had resulted in complete dilatation and effacement of the cervix. Denudation of mucosa, skin, and scar tissue lining a small vaginoperineal fistula resulting from a previous confinement, preceded the repair of the episiotomy.

Interest lies in the long stormy puerperium which may be divided into a short first and a long second period of hyperpyrexia. Initiated by a rise to  $101.6^{\circ}$ , the first phase gave the signs of sapremia and subinvolution and yielded to the usual treatment in eight days, although the fundus remained near the level of the umbilicus for sixteen days. The symptoms in this first period were lower abdominal pain, tenderness over the uterus, and foul-smelling discharge coming through the cervix.

In the second phase there were also pain and tenderness in both lower quadrants while the new rise in temperature, beginning on the thirteenth day, continued with wide remissions until it reached the height of  $104.4^{\circ}$  on the twenty-sixth day. During the rise a transfusion of 700 c.c. whole blood had given only transient improvement. But at the peak of the fever an intramuscular injection of 5 c.c. of sterile milk was given and was followed in twenty-four hours by a fall to  $102.4^{\circ}$  and in forty-eight hours by drop to  $100.6^{\circ}$ . During the prolonged gradual defervescence a second transfusion of 500 c.c. of blood, and 10 more intramuscular milk injections of 10 c.c. each were given.

Examination during the second phase showed perineum and cervix healthy, corpus the size of five to six months' pregnancy, boggy or elastic, retrocessed and displaced to right where it was adherent to an enlarged, indurated, tender right appendage. Before the first transfusion the blood culture was sterile, the Hgb. 50 per cent with R.B.C. 3,500,000, W.B.C. 17,000, and polymorphonuclears 85 per cent. At the height of the fever the white count was 21,400 with 92 per cent polymorphonuclears; and the sedimentation was 100 mm. in the first hour. Gradual improvement during the next three weeks; mother and baby discharged on fifty-second day.

Examination in the Obstetrical Follow-Up Clinic revealed, on the first visit three months postpartum, pain and tenderness in right lower abdomen, uterus enlarged, anterior, and pulled over and fixed to the right appendage which was indurated and tender. This was confirmed on the second and third visits; and at final visit, on Nov. 6, 1930, when the patient was referred to the Gynecological Division, the tender mass now palpable abdominally and vaginally.

Admitted Nov. 10, 1930, to the Gynecological Ward, complaining of "nagging

\*Presented at a meeting of the Obstetrical and Gynecological Section of the New York Academy of Medicine, November 24, 1931.

pain," and a lump in the lower abdomen and loss of strength, the patient looked slender but of better color. The uterus was now found displaced to the left by a nontender semicystic, partly fixed mass high in the right pelvis, seeming to lie just under the skin. Hgb. 80 per cent, R.B.C. 4,000,000, W.B.C. 10,000 with 68 per cent polymorphonuclears. After one week's observation the preoperative diagnoses were as follows: tuboovarian mass or abscess; degenerating myoma; herniated myoma or adnexal mass.

At operation no hernia was found, the peritoneal cavity contained small amount of clear fluid and numerous fibrinous adhesions. Corpus uteri normal but displaced to left. Right adnexa made up a cystic mass 10 cm. in greatest diameter, filling the right upper pelvis and extending into the iliac fossa; it was firmly adherent to uterus, anterior abdominal wall and urachus; a loop of ileum was attached to it and the whole covered over by adherent omentum. Appendix 12 cm. long, prolapsed into pelvis, and thickened. Left adnexa normal. Right salpingo-oophorectomy, appendicectomy, and separation of adhesion was performed. During the removal of the cystic mass, it was accidentally ruptured, allowing spillage of thin brown fluid which was unfortunately not cultured. Closure without drainage.

Pathologic examination of the tuboovarian mass showed numerous small hemorrhagic cysts and a large cyst over which was stretched the edematous tube. Microscopically the ovarian parenchyma was nearly all destroyed by an intense inflammatory infiltration with confluent abscesses and much necrosis. No epithelial lining found in the cystic compartments. Pathologic diagnosis: chronic purulent salpingo-oophoritis and chronic appendicitis.

Postoperative convalescence was featured only by an infected subcutaneous hematoma near the upper angle of the incision. The discharge, from which *B. coli* was cultured, cleared up rapidly. Examination at discharge on twenty-fourth day showed abdominal incision, uterus and left adnexa normal, and the patient relieved of her symptoms. Seen at Follow-Up Clinic, January 21, 1931, patient states she feels stronger, does all her own work, and has no complaint. Bowels regular. Examination shows firm abdominal wall, cervix clean, corpus uteri normal in size, shape, position, and mobility; left adnexa prolapsed, slightly enlarged. No tenderness in either side of pelvis.

This case illustrates:

1. A severe and refractory secondary anemia of pregnancy, possibly aggravated by latent adnexal disease. The pathologic report indicates cystic disease of the right ovary; but the previous general and menstrual history did not point to it.
2. A stormy puerperium with subinvolution, sapremia, parametritis, and inflammation of the uterine appendages.
3. The avoidance of intrauterine examination, irrigation, or curettement; and the long delay before operative intervention, allowing a conservative procedure with easy recovery in spite of gross spillage of infective material.
4. The apparent benefit of repeated milk injections and blood transfusions.
5. The possible bearing of the operative delivery, the plastic repair of vaginoperineal fistula, and the prolonged anesthesia on the subsequent course.

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## ACUTE INTESTINAL OBSTRUCTION COMPLICATING LATE PREGNANCY\*

GEORGE GORDON BEMIS, M.D., NEW YORK, N. Y.

*(From the Clinic of the Woman's Hospital)*

**A**CUTE intestinal obstruction is a relatively infrequent complication of pregnancy. At the Woman's Hospital in the State of New York it has occurred twice, including the case to be reported, in 15,000 obstetrical patients. In the American and British literature, from 1900 to the present time, thirteen cases have been reported. The condition seems sufficiently unusual to warrant reporting this case.

The patient, Mrs. L. N. E., applied for prenatal care June 14, 1929. She was twenty-nine years old, married three and one-half years and a primipara. The past history was essentially negative, except that at the age of fourteen her appendix had been removed, because she was told she had chronic appendicitis. The postoperative course had been uneventful, and the wound had healed by primary union. She had no abdominal discomfort since the operation.

The general physical examination on the first visit was negative except for a lower right rectus scar, the site of the previous operation. Pelvic examination revealed a normal pelvis. The uterus was symmetrical and enlarged to the size of a twenty-two weeks' pregnancy. The adnexa were normal.

The patient was seen every two weeks from the time of her first visit in June until November 16. She had no unusual complaints and in fact stated on November 16, the day before the onset of her present illness, that she never felt better in her life. On the morning of November 17 her husband phoned about 7 A.M. that his wife had awakened at 3 A.M. with a severe pain in the lower right side of her abdomen. The pain had persisted and she had not been able to sleep. Further questioning revealed her bowels had moved poorly the preceding day. She had not vomited or felt nauseated. An hour later the patient was seen in her home. She was lying in bed and appeared to be only moderately uncomfortable. The temperature and pulse were normal. Abdominal examination revealed a pregnant uterus extending up to the level of the costal margin and moderate tenderness in the lower right abdomen just lateral to the abdominal scar. There was no apparent distention. A mild catharsis and a high enema were prescribed on the presumptive diagnosis that the discomfort was probably due to an intestinal stasis. The results from the enema were poor, but the patient was relieved. She reported the next morning that she had no pain and had rested well that night. In the evening of the same day she again developed severe pain in the lower right abdomen. The patient was seen within a short time. She appeared extremely uncomfortable tossing about in bed and complaining greatly of the pain in her right side. There was definite generalized abdominal distention and the tenderness in the right side of the abdomen was more marked. The bowels had not moved during the day and the return flow from two enemas had been clear. A diagnosis of possible intestinal obstruction was made, and the patient was immediately taken to the hospital for further observation and treatment with the hopes that the obstruction could be relieved without an operation. Conservative measures failed, and after twenty hours it was apparent that the distention was becoming more pronounced and the pain more severe. The patient's general condition was good and it was decided to operate.

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\*Read before the Section on Obstetrics and Gynecology, Academy of Medicine, November 24, 1931.

A lower right rectus incision was made lateral to the old scar and the peritoneal cavity opened. The practically full-term pregnant uterus made exploration of the abdomen very difficult. However, the obstruction was localized in the ileocecal region. Five distinct bands of firm adhesions were found forming a constricting band across the cecum just above the ileocecal junction. The cecum and small intestine proximal to this constricting band were greatly distended. These adhesions were divided and the obstruction relieved. The abdomen was closed and the patient returned to her room in good condition.

Twenty hours later the patient passed gas and a small amount of fecal material through the rectum. From this time on her condition improved rapidly. On the third day the temperature and pulse were normal and the abdominal distention was entirely relieved. The wound healed by primary union. On the fifteenth postoperative day the membranes ruptured spontaneously and labor began thirty-six hours later. At the end of the twelve hours of relatively easy labor, the cervix was fully dilated and the head was engaged. The patient was immediately delivered by mid-forceps of a seven pound boy.

The postpartum course was uneventful, and the patient and baby were discharged from the hospital on the fourteenth day after delivery.

This case is of interest in that it emphasizes:

1. The necessity of careful examination and evaluation of acute abdominal symptoms developing during pregnancy and the importance of always excluding an acute surgical condition,

2. If an acute surgical condition exists, it should be treated with as conservative an operation as is possible,

3. It would seem better judgment not to interfere with the pregnancy, as it subjects an acutely ill patient to additional strain.

121 EAST 60TH STREET.

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## REPORT OF A CASE OF CONGENITAL VULVOVAGINAL ANUS

R. K. PACKARD, M.D., AND J. D. KIRSHBAUM, M.D., CHICAGO, ILL.

*(From the Surgical Service of the Woodlawn Hospital)*

IN REVIEWING the literature we were able to find only one case simulating ours in that the anomalous condition of a congenital vulvovaginal anus existed without the knowledge of the patient. This was made possible because of the absence of any fecal incontinence. Most of the cases reported had to have some type of operation to correct the fecal discharge into the vagina. Our case required no operation because of the perfect functioning of the anus although it was in the vestibule of the vagina.

Some of the titles attached to this congenital malposition of the anus are: atresia ani vaginalis, anus vestibularis, atresia ani hymenalis, vaginal anus, and vulvovaginal anus. Pankow states that the defect should really be termed vestibular anus since it gives a more descriptive understanding of the term applied.

Vaginal anus abnormalities are the most common of all the congenital defects of the anus and rectum. It is estimated that it occurs in 40 per cent of the cases where the rectum may open either into the urethra,

bladder, uterus, or vagina. It is said that some type of anorectal malformation occurs in 1 out of every 7,500 to 10,000 births. Collins, at the Rotunda Hospital, Edinburgh, found only 1 case in 16,000 births. Winckel found 1 case in 12,000 babies at the Dresden Hospital. A number of cases undoubtedly go unrecognized because the baby dies in the first twenty-four hours, due to atresia elsewhere along the gastrointestinal tract. Morgagni reported a case of a woman living to be one hundred years old with a vestibular anus and she never knew of her defect. In 66,654 deliveries in Vienna and Dublin Lying-In Hospitals, there were only 3 cases of imperforate ani. Our case represents 1 case of congenital defect of the anus in 1684 births at the Woodlawn Hospital, Chicago.

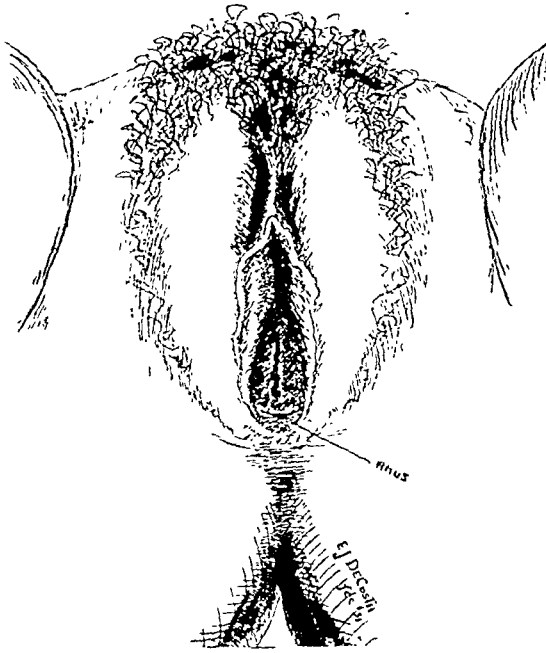


Fig. 1.

Buckmaster<sup>2</sup> reported 52 cases, 14 of which were adults, before the American Gynecological Society in 1894. Brenne<sup>1</sup> reported 3 cases and Dotti,<sup>4</sup> Spivak,<sup>17</sup> Christopher,<sup>3</sup> DeSedilus,<sup>7</sup> Mondon,<sup>13</sup> and Paschal<sup>15</sup> all reported cases. Orvall Smiley<sup>14</sup> saw a patient with this defect in labor who delivered a living child with the aid of forceps, but received a deep laceration. Dwight's<sup>5</sup> case was a virgin, thirty-two years of age. Rautzou,<sup>16</sup> Jayne,<sup>9</sup> Morris,<sup>11</sup> and Tubby<sup>18</sup> each saw a case in a child. Duros<sup>6</sup> reported 14 cases, 5 of which were adults. Vecchione,<sup>21</sup> Lebrun,<sup>10</sup> Gouriane,<sup>8</sup> and Thompson<sup>19</sup> each reported cases in adults. Since 1894 there have been 22 cases reported.

Mrs. G. W. P., aged twenty-eight years, a primipara, was admitted to the Woodlawn Hospital May 16, 1930. The patient was apparently in perfect physical condition with a normal L.O.A. presentation. A nurse was instructed to give the pa-

tient an enema; she reported that she was unable to do so because of her inability to find the anal opening. Careful examination revealed the absence of the anal opening in the normal position; instead the anus was located in the vestibular portion of the vagina. Upon questioning the patient she was not aware of any defect and had normal bowel movements and intercourse without any knowledge of her defect. Careful questioning of the mother revealed that she had never noticed, during the patient's infancy or childhood, any defect in the anal opening. There was sufficient sphincter muscle to give perfect control. The anal opening was sufficiently external in the vestibule so that there had never been any vaginal contamination from feces.

Cesarean section was advised as the only safe method of procedure to preserve the rectum intact. Accordingly, this was done and the patient made an uneventful recovery. She was discharged May 29, 1930, thirteen days after her operation.

From the history of the patient, obtained from herself and from her mother we learned that, as she had never had any bowel trouble or constipation in infancy, childhood, or adult life, there had never before been an attempt to give her an enema. This patient had been given one vaginal examination previous to entering the hospital but at this examination the congenital defect was not discovered.

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526 EAST SIXTY-FIRST STREET.

# Society Transactions

## OBSTETRICAL SOCIETY OF PHILADELPHIA

STATED MEETING OF JANUARY 7, 1932

DRS. L. AVERETT, W. SUSSMAN AND D. ZIMRING presented a paper on  
**Spinal Anesthesia.** (For original article see page 339.)

### DISCUSSION

DR. WAYNE BABCOCK.—I would like to say regarding the abducens paralysis mentioned, that in our first 2,000 spinal anesthetics, we had 6 cases of internal squint. Quite uniformly there was an incubation or prodromal period of six or seven days, during which the patient had severe headache and perhaps other evidence of meningeal irritation. The paralysis lasted from a few days to two months and followed the use of imported solutions. Some of these, on being tested abroad, were found to contain bacteria. In two lots of ampules containing glucose, a heavy growth of a fungi developed on standing. Discarding these ampules and using solutions containing a small percentage of alcohol, we have since had over 20,000 spinal anesthetics without another abducens palsy. I believe, therefore, that the paralysis is due to infection from the injection of a contaminated solution.

Postanesthetic headache which, for years, has been rare in our experience, was common in the early years, and also seemed to result from the use of improperly prepared solutions. Without changing the formula or the needle used, an incidence of 30 or 40 per cent of headaches would practically disappear when a new laboratory prepared the drug. At the present time, if over 3 or 4 per cent of one's patients are having headaches from spinal anesthesia, I think he should carefully review his technic and have a new lot of the drug prepared with great care. Only freshly prepared and triply distilled water should be used for solutions, since the violent reaction following the intravascular injection of old distilled water may be paralleled with intradural injections. Likewise, needles, syringes, and containers should be kept apart and used only for the spinal injection. They should be scrupulously clean; and should be boiled in freshly distilled water only and not with other instruments. We do not allow anyone except the one person giving the injection to handle the sterile syringe or needle, nor does this person touch the ampule. After having seen a rather well-known orthopedic surgeon die from purulent meningitis following a diagnostic spinal puncture, I shudder when I see operating nurses promiscuously handling the sterile spinal outfit together with ampules, perhaps with a gummed paper label in place, that have only had a brief submersion in alcohol.

Regarding the needle: A rather blunt obtuse-pointed needle has been advocated, because it cuts a little "trap door" in the dura and is claimed to cause less leakage of cerebrospinal fluid. If you experiment with a membrane, you will find that sharp-pointed needles cut as good or perhaps even a better "trap door." While not advocating a needle larger than 20 gauge, I am sure that spinal leakage is less important than what is injected as a cause of the headache.

The hypertension from spinal anesthesia has perhaps also been overrated. A fall in systolic blood pressure to 60, is seen almost daily, and we do not consider it serious unless the patient is otherwise in a serious condition or has a damaged myocardium. Indeed, we are more afraid of the hypertension and tachycardia

produced by ephedrin. We have not used ephedrin except in a few experimental cases. Some patients have an idiosyncrasy toward it. In the 12 deaths occurring around Boston, after about 200 injections of spinocaine, Size attributed 2 of the fatalities to ephedrin. Other deaths were at times preceded by convulsions. The two at the Jackson (Wisconsin) Clinic also suggest the danger of ephedrin.

I think it wise to watch the patient under spinal anesthesia very closely, and to depend for stimulation on suprarenin, in the rather rare case in which stimulation is really necessary.

While in obstetrics, spinal anesthesia is of great advantage, it also carries a special danger to the pregnant woman. For complete peritoneal anesthesia, the area of analgesia should reach the fifth rib; because we cannot accurately control the diffusion of the drug, at times the third or second rib will be reached. Thus, most of the external muscles of respiration are paralyzed and the patient is compelled to breathe almost entirely with the diaphragm, supplied by the third, fourth and fifth cervical roots. The average patient gets along very well in this way. With a large pregnant uterus, or large abdominal tumor in the upper abdomen, the diaphragm is so fixed that it cannot well move, and so with a high spinal anesthesia, the patient may be unable to breathe and may die unless artificial respiration is used or the uterus quickly emptied. However, low spinal anesthesia can be given which will anesthetize the birth canal with little effect on the blood pressure and no effect on the respiration. The obstetrician who attempts to use spinal anesthesia should carefully study the technic for preventing the drug from reaching the thoracic spinal roots. A light solution of the anesthetic given with the patient sitting up, gravitates upward, and may produce too high an effect; injected with the patient horizontal and on the side, it tends to rise to the anterior convexity of the lumbar curve as the patient is turned on the back, producing a rather low anesthesia. If the patient is now turned on her face, a higher gravitation occurs into the thoracic region, as the dorsal spinal curve is now dependent. The effect is not due to the relative position of the dorsal and lumbar roots, as has been thought. If, on the other hand, one is injecting a solution heavier than the cerebral spinal fluid, the anesthetic tends to gravitate to the thoracic region with the patient supine. Thus, if you use a drug dissolved in cerebrospinal fluid, or a heavy solution, wait ten minutes before the head is lowered, or the Trendelenburg position used, that the solution may become fixed and not gravitate cephalad, nor should you use a dose too large to be fixed by the spinal system. By a controlled large dose, the duration of anesthesia may be lengthened up to three hours irrespective of the local anesthetic used; but this necessitates especial care.

I believe that the death described by Dr. Averett was not due to the anesthetic. This patient had a high blood pressure and the symptoms were not those of a spinal collapse.

DR. AVERETT (concluding).—Our experience with ephedrin as a prophylactic for the drop in blood pressure in spinal anesthesia, has been uniformly good. We use it only once, no more than  $\frac{3}{4}$  of a grain, and if vasomotor stimulation is necessary, we resort to adrenalin.

Dr. Babcock's experience of having had methyl alcohol used in place of ethyl alcohol in the preparation of his spinal anesthetic cannot occur in our technic, as we dissolve the novocaine crystals in the cerebrospinal fluid only.

DR. LIDA STEWART-COGILL reported a case of **Full Time Abdominal Pregnancy**.

Mrs. B., aged twenty-three years, gravida ii, registered at the prenatal clinic at the Woman's College Hospital, August 11, 1931. The date of her last period was



uncertain, confinement probably due October 1, 1931. Upon abdominal examination the fetal ovoid was longitudinal, the abdomen was symmetrically enlarged, fetal movements were not more active or more distinctly felt than in a normal case and did not give the patient any discomfort; in fact, she was very comfortable, having no complaints. The fetal heart rate was 140, good character, and was heard in the right lower quadrant. What was thought at this time to be the fundus of the uterus was felt halfway between the umbilicus and the ensiform process. Patient came regularly to the clinic; she remained comfortable, the abdomen continued to enlarge symmetrically, and the fetal heart remained good until October 3, 1931, when no fetal heart sounds were obtained.

Patient entered the hospital October 16, 1931, complaining of feeling sick, but not in any pain. Fetal ovoid extended to  $2\frac{1}{2}$  cm. below the ensiform process, and the baby was in right occipitoposterior position. Fetal heart was not heard.

Having no reason to suspect an extrauterine pregnancy and believing her to be overdue, efforts were made to induce labor. After several unsuccessful attempts with medical treatment, such as castor oil, quinine, and strychnia, a bougie was tried, without an anesthetic. The cervix was only moderately soft, barely admitting the tip of the finger. The bougie could be passed only three inches into the uterine cavity.

Realizing there was some serious abdominal condition present, we questioned the patient closely and she stated that when five months pregnant, she had a moderately severe pain in her side and felt faint for a few minutes only, otherwise she had never had any discomfort. Under gas anesthesia a vaginal examination was made and a small cord-like body was found on the left side of the pelvis resembling the uterine body; also a uniformly enlarged cystic mass filled the pelvis and extended upward above the umbilicus. The presenting part could not be felt.

The abdomen was opened by a low abdominal incision; the fascia and muscles were split, and in cutting through the peritoneum a thickened sac almost the thickness of the uterine muscle was encountered which was adherent to the parietal peritoneum. This was cut through and the bulging membrane was ruptured, whereupon greenish yellow fluid escaped. This thickened sac accounted for the fact that the fetal parts were not more distinctly felt on palpation and for mistaking the wall of the sac for the uterine wall. A macerated baby, evidently at full term, was extracted from this well-formed sac. The placenta had been entirely detached, except at a line along the posterior wall of the sac and toward the right side. The placental blood vessels extended toward the posterior wall of the pelvis in a fan-shaped manner. These vessels were ligated by interlocking chromic catgut sutures and the placenta with its cord was removed. There was practically no bleeding, as the fetus had been dead a sufficient length of time for blood vessels and placental sinuses to be well thrombosed and closed.

The sac was wiped dry and left in the abdominal cavity, as it was firmly adherent to the abdominal structures, the edge of the sac wall and peritoneum were sutured together with continuous chromic catgut. The remaining portion of the abdominal wall was closed in the usual manner; the patient was returned to bed in excellent condition, and the incision healed by first intention. Beginning on the eleventh day after operation, the patient had a daily rise in temperature to  $101^{\circ}$  F., gradually falling by lysis. On abdominal palpation an area of induration not sensitive to pressure could be outlined on the right side; this was evidently due to absorption of the sac which had been left in the abdominal cavity. Patient left the hospital in good condition.

In this case had the fetus been living or the death recent, the manner of dealing with the placenta and sac might have been different, due to danger of severe hemorrhage.

## DISCUSSION

DR. GEORGE M. BOYD.—I have observed two similar cases myself. The first occurred thirty-five years ago, and was operated upon late, believing the delay might thus best conserve the mother's life. However, she had profuse hemorrhage after the operation and died.

The second case I reported to the Society in February, 1930. The patient came to the hospital in 1929, at term. The head was in the pelvis—so much so that it could very easily have been mistaken for a normal pregnancy.

In 1930, such a mistake was made in this State. The doctor punctured the vaginoperitoneal septum and gestation sac, removed the baby by its feet, and then proceeded to deliver the placenta. This resulted in the protrusion of the intestine and the patient was sent to the hospital. She died in a few days of hemorrhage and infection.

The chief point of interest is how to handle the placenta. In my successful second case the placenta was attached to the omentum and the inner side of the right broad ligament. Hemostasis was accomplished by ligating the branches of the ovarian and uterine vessels and in that way we could remove the placenta with very little bleeding.

DR. COLLIN FOULKROD.—During the past year I have had the opportunity of observing an abdominal pregnancy from the beginning. I operated upon this patient some years ago for an extrauterine pregnancy in the left tube. In the present pregnancy at the time of tubal abortion there was some evidence of concealed hemorrhage but she had no vaginal hemorrhage, so I did not operate then. She was very anxious for a child and knew she was pregnant. She had two masses in the pelvis. We did not know whether we were dealing with a pregnancy complicated by a tumor. The child died in the seventh month.

I have operated upon two similar cases, and in each it seemed to me that the wiser plan was to wait until the placenta had atrophied, so I waited for six weeks. At the time of operation there was a very thin sac, and numerous adhesions to the intestines. The placenta dipped over into the lower reaches of the pelvis, and I was unable to get it all out. The pelvis was drained and the woman recovered. In the other case the child was dead. The pelvis was drained, in that case also the woman recovered.

DR. MARGARET C. STURGIS read a paper entitled **Hysterosalpingography in Sterility Studies.** (For original article see page 355.)

## DISCUSSION

DR. JACOB VASTINE.—The shadow of the uterus as seen on the roentgenogram should be smooth, and when we find irregularity it is customary to diagnose it as endometritis. Whether it is a hyperplasia, or what the process is must be determined by the gynecologist.

DR. ANN GRAY TAYLOR presented a report of **Four Cases of Dystocia Following Trachelorrhaphy.**

In the Woman's Medical College Maternity Hospital of 4 patients who had a trachelorrhaphy only 1 delivered spontaneously.

CASE 1.—Mrs. B, colored, came to the prenatal clinic October, 1928, when four months pregnant. In April, 1927, two months after her sixth delivery, she had a trachelorrhaphy and perineorrhaphy. This pregnancy was normal except for moderate hypertension which she had also had with the previous pregnancy. Labor was spontaneous and normal in every respect.

CASE 2.—Mrs. J. B., white, aged thirty years, came to the prenatal clinic April, 1929. General history was negative. Her first labor, twelve years previously, was normal; second labor, ten years previously, resulted in a forceps delivery; third labor, nine years previously, was spontaneous. In August, 1927, she had had a trachelorrhaphy and perineorrhaphy with normal convalescence. This pregnancy was normal throughout. Labor began about three days before the expected date and in spite of advice, the patient did not come to the hospital until four hours after the pains began. Rectal examination showed the cervix to be well obliterated and about one finger dilated, the external os having the consistency of a cartilaginous ring. As the condition remained stationary for two hours, a cesarean section was done; convalescence was uneventful. In March, 1931, the patient again came to the prenatal clinic; no unusual symptoms occurred during pregnancy. Labor at the expected date showed the same condition of the cervix after three hours of good uterine contractions. Cesarean section was done. Convalescence was normal.

CASE 3.—Mrs. A., white, aged thirty-three years, was first seen January 6, 1929. The last regular period was September 12, 1928, with one which lasted for two days beginning September 26. Her first labor had been a forceps delivery nine years before; second and third labors were spontaneous. Trachelorrhaphy and perineorrhaphy were done three and a half years ago. The present pregnancy was uneventful. On June 10, 1929, the pains began at 5 P.M. At 9 P.M. rectal examination showed the cervix well obliterated, one finger dilated, with line of previous incision thick and firm. The patient had planned to be delivered at home, so did not readily consent to go to the hospital. Three hours later vaginal examination at the hospital revealed the same condition of the cervix. At the time the cesarean section was done the patient had been seven hours in labor with contractions occurring every two minutes for the last hour. She had an uneventful convalescence.

CASE 4.—Mrs. P., gravida viii. When first seen October 3, 1929, she was very apprehensive and unhappy. The previous labors had been long, the fourth instrumental, the rest spontaneous. In August, 1927, because of a lacerated cervix and perineum and retroflexion of the uterus, also hydrops of the gall bladder, with stone in the cystic duct, she had had a trachelorrhaphy, perineorrhaphy, abnormal suspension of the uterus, and cholecystectomy. Her last period was June 8, 1929. On November 19 she had a severe cutting pain on the right side of the abdomen which lasted about ten minutes. On November 20 she had a similar attack of pain on the left side. Throughout this pregnancy the abdomen was unusually sensitive. On February 26, 1930, she had severe pain above the symphysis. On February 27, 1930, she had pain in the back and on the right side. Labor actually began February 28, 1930, about two weeks before the expected date. After about four hours of labor, the cervix was obliterated, one finger dilated, and the line of scar tissue was prominent. Cesarean section was done with the resection of tubes at the patient's request. Normal convalescence.

## DISCUSSION

DR. WILLIAM R. NICHOLSON.—While I have never seen a case of cervical repair, or even cervical amputation, resulting in the necessity for cesarean section, I nevertheless feel that the danger of such an occurrence following repair is very real. I have always held the opinion that it was much better to do no suturing of the cervix, following delivery, unless there was bleeding, and also have always felt that operations upon the cervix during the childbearing period must be done with great care, for fear of production of dystocia in succeeding pregnancies. Since the advent of the cautery, my opinion in this matter has been greatly strengthened. It is not the fact of there being a healed laceration which threatens a woman's

well-being, but the presence of ectropion or erosion of the cervix. By means of the cautery, these two mentioned conditions can be very rapidly and certainly eradicated.

Moreover, the immediate repair after delivery does not obviate the development of ectropion or erosion later on. I have had occasion to examine cases subsequent to immediate repairs done after labor by colleagues, and again state the above as an actual fact, and also that the dangers incident to the immediate repair of the cervix are manifold.

In a well-organized hospital, repair of the cervix can be done, probably, with a low incidence of morbidity, but if this be attempted outside of hospitals, and I think it is frequently forgotten that the majority of deliveries occur outside hospitals and probably always will, the results will be an increased morbidity, and possible mortality from infection.

I believe that in presenting papers to special societies, such as this, the writer should definitely state whether, in his opinion, the procedure advocated is applicable to house obstetrics or not, since, otherwise the influence of articles presented before such special societies may be very prejudicial to the best interests of the patient. Moreover, the general practitioner who still delivers by far the greatest number of women, is absolutely unfit, by training and equipment, to sew up a lacerated cervix immediately following delivery. In the cases reported in which cesarean was necessary, the use of the cautery to heal any erosions or ectropion following previous pregnancies, would have probably saved these patients from a major operation.

DR. STEWART-COGILL.—The best treatment of lacerations of the cervix is one of prevention—namely, following the rule of not attempting to deliver the infant vaginally until the cervix is completely dilated and obliterated.

If a primary repair of the cervix is performed and in such manner as to resemble, at completion of operation, a hypoplastic type of cervix, in a subsequent delivery it is likely to produce a dystocia often resulting in cesarean section or deep laceration. The Sturmdorf operation is not desirable during the childbearing period, as complications similar to those previously mentioned are likely to occur.

DR. CATHARINE MACFARLANE AND DR. M. ELIZABETH HOWE read a paper on **Cancer Prophylaxis**. (For original article page 406.)

#### DISCUSSION

DR. P. BROOKE BLAND.—The former practice of routinely submitting all patients to unskilled vaginal examination during labor, with the irresistible tendency to dilate manually and slip the attenuated cervix over the presenting part and incidentally traumatize the structure thereby, was unquestionably responsible for much cervical damage, with its train of immeasurable sequelae. It is not possible to tell how much this wholly unnatural practice has cost in morbidity, both immediate and remote. With less injudicious vaginal manipulation, both manual and implemental, so poignantly expounded in the teachings of obstetrics today, the incidence of cervical injury should materially be reduced.

From the foregoing, one seems almost justified in claiming, as pointed out by Dr. Macfarlane, that the solution of the problem, as far as prevention is concerned, rests far more with the obstetrician than with the gynecologist. In the past he has, I fear, fallen somewhat short in this respect.

DR. CHARLES S. BARNES.—One very striking fact, in the presentation by Dr. Macfarlane, is that 15 per cent of those who were found to have cervical cancer had no history of miscarriage or labor. We have been teaching that it is the rarest occurrence that a woman develops cancer of the cervix unless she has had one of

these experiences or some other traumatism. I should like to ask Dr. Macfarlane if she knows of any diagnosis of traumatism that was made in those cases; e. g., cervical dilatation.

I do believe that it will become as much of a routine measure to repair a lacerated cervix as it has been to repair the perineum, and that it will be considered just as much the duty of the obstetrician to do it. The chief reason against it has been, of course, the danger of infection; but now that we are doing so much in hospital environment, that risk is greatly minimized, and I should like to endorse that particular feature in Dr. Macfarlane's paper.

DR. COLLIN FOULKROD.—An amazing personal experience of the last ten years is that since I have made rectal examinations entirely, I have found very few lacerations. In the primiparous patient the cervix relaxes and retracts very much more evenly than in the multiparous. The tears that cannot be repaired are the ones that finally lead to cancer. In the multiparous patient around the edge of the portia vaginalis there are usually numerous stellate cracks and often eversion of the mucous membrane of the canal; these tears cannot be repaired but can be healed by the cautery in the postnatal examinations. Such cauterizations should be persisted in until all erosions are healed and eversions folded in.

As to the repair during the childbearing period, I believe, with many obstetricians, that if we can cure the cervix by cauterization, and leave the repair alone, we are saving the women from cesarean section or a much more seriously lacerated cervix.

DR. JOHN A. McGLINN.—I have no objection to the immediate repair of the cervix, because I believe that anything that will prevent the development of lesions of the cervix which predispose to cancer, is wise. But I doubt very much if the routine repair of the cervix after labor is absolutely necessary.

I make it a routine practice never to discharge an obstetric patient until the cervix is entirely healed. Since high forceps are practically never used and mid-forceps but rarely, and large doses of pituitrin have been entirely discarded, it is amazing how infrequently we see a lacerated cervix. Of course, we do see eversion, erosion, and infection.

I am firmly convinced that cauterization of the cervix or coning out of the cervix is far better than either repair or amputation of the cervix. I have practically discarded all operations on the cervix and confine myself to cauterization or coning.

DR. DANIEL LONGAKER.—It is the duty of the obstetrician who sees these cases antenatally and postnatally, not to discharge a woman until her cervix is free from erosion, healed, and the entire surface is covered with squamous epithelium to the external os.

Another more important point is that ample time be given, so that the cervix is not only dilated but retracted and the head completely extruded into the vagina before interfering instrumentally.

Departure from this rule frequently leads to the need for primary repair. In the diagnosis of the so-called erosions a proper light attached to a correct speculum such as the Cameron light and speculum, gives definiteness to the diagnosis.

DR. MACFARLANE (concluding).—In reply to Dr. Barnes' question I would state that there was no history of operative procedure in any of the nulliparous patients with cancer of the cervix.

# OBSTETRICAL SOCIETY OF PHILADELPHIA

MEETING OF FEBRUARY 4, 1932

DR. EMIL NOVAK, of Baltimore, Md., presented a paper entitled **Certain Endocrine Factors in Menstruation and Menstrual Disorders.** (For original article see page 319.)

## DISCUSSION

DR. BARTON C. HIRST.—It was about 1906 that my first experiments were made with ovarian extracts, by making a glycerine extract of the fresh corpus luteum from human ovaries. The response to injections was sometimes quite remarkable in cases of amenorrhea, sterility and the artificial premature menopause.

One young woman from whom, according to the operating room records, both tubes and ovaries had been removed, came back to the dispensary with symptoms of the precipitate menopause; after a few injections of the glycerine extract of the corpus luteum she disappeared for a while and then returned pregnant! Naturally a scrap of ovary, overlooked at the operation, had been activated.

Dr. Novak gave what was to me a new lesson on this factor of bleeding from the anterior lobe of the pituitary. If this theory is correct, how can we explain the results that we are unquestionably getting from the injection of anterior lobe extracts in women with the atypical menorrhagia of puberty, maturity and the menopause. Some additional information on this point from laboratory workers would be most welcome to the clinician.

DR. BROOKE M. ANSPACH.—Some time ago before this Society, Dr. Hoffman and I presented a plan of treatment. I wish to mention it briefly and ask Dr. Novak whether he approves and how his own plan differs. In the first place, we start out with the understanding that irregular bleeding, which many of our cases have presented, is not menstruation in the true sense; that is, bleeding which follows ovulation and the formation of a corpus luteum. We may speak of it as menstruation without ovulation, or, more accurately as functional bleeding without ovulation and corpus luteum formation. Some women complaining of sterility who have regular bleeding and who therefore would be supposed to ovulate, as a matter of fact do not ovulate and do not have a corpus luteum. We have preferred to postpone the administration of the available hormones and other therapeutic measures in our cases until we have had an opportunity to determine as nearly as we can just where the trouble lies. In every case therefore we first make the usual general and endocrine estimation of the patient. Tests are then performed to determine the female sex hormone and anterior pituitary hormone content of the blood. The results of these tests together with the information gained from a study of a strip of endometrial mucosa taken just before the period is due form the basis of our final estimate of the patient's condition. We have come to regard this histology of the mucosa as perhaps the most reliable index of ovarian and pituitary function. If the studies point to a lack of folliculin, we administer theelin as substitution therapy. If, as in cases of functional menorrhagia, we find an absence of corpus luteum formation, indicating a lack of progesterin, we make use of the anterior pituitary luteinizing hormone as mentioned by Dr. Novak. We have up to now had about 40 cases of this type and the result of the treatment has been almost uniformly excellent and apparently curative, although the cases are of much too recent origin to speak of them as cures. In amenorrhea, due to glandular imbalance, we have had little success with the use of theelin and anterior pituitary luteinizing substance, but thyroid administration and x-ray stimulation of the pituitary have given favorable results in a few instances. For the cases of amenorrhea we believe that a potent extract of the anterior pituitary is required.

DR. CHARLES MAZER.—The conception of duality of the anterior pituitary sex hormone is still debatable. With the exception of Claus, no one has thus far produced definite evidence to justify the assumption that the follicle-ripening hormone differs biologically from the so-called luteinizing hormone of the anterior pituitary lobe. The available anterior pituitary sex hormone-products are capable of evoking both phases of the ovarian cycle—follicle-ripening and luteinization. The effect, in my experience, depends entirely on the quantity employed, the species-susceptibility of the animal and the time at which the ovaries of the animal are removed for microscopic examination.

From the clinical standpoint the question of duality of the anterior pituitary sex hormone is of utmost importance as the luteinizing hormone would be clinically applicable only in cases of functional uterine bleeding and not in the treatment of amenorrhea due to failure of development of the primordial follicle.

The premenstrual phase of the human cycle is not governed solely by the corpus luteum hormone, progesterin. In fact, the corpus luteum produces larger quantities of female sex hormone than the mature follicle, as evidenced by the concentration of the hormone in the blood of women during the height of corpus luteum function—premenstruum. Moreover, Allen has shown that implants of corpora lutea into castrated rodents are more efficient in producing estrus than implants of follicular tissue.

Hartman's suggestion that the anterior pituitary lobe produces a hormone which, independent of the ovaries, is capable of producing uterine bleeding requires corroboration, as the bleeding he induced in the hypophysectomized, castrated and non-castrated infantile monkeys, in which estrin failed to produce bleeding, was only microscopic. The ability of anterior pituitary sex hormone to produce congestion which may result in microscopic uterine bleeding without specific changes in the uterine mucosa was demonstrated by Wagner and Zondek on women who received injections of Prolan prior to laparotomy.

DR. JACOB HOFFMAN.—Following Dr. Novak's suggestion, we have had uniformly good results in the use of this hormone in 40 cases of functional menorrhagia associated with endometrial hyperplasia, especially in young women.

Dr. Novak's theory as to the cause of dysmenorrhea is worthy of serious thought. In accordance with it, one would expect to find an excess of folliculin, the stimulating factor, and a deficiency or total absence of progesterin, the inhibitory factor, at the time when the pain is present. In our studies, we have found the endometrial picture to be the most reliable index of the activity of these two hormones. Would it not be a good plan to examine the endometrium in all cases of dysmenorrhea of this type? If the endometrium does not show premenstrual changes and instead is hyperplastic, it would explain the pain on the basis of an excess of the follicular hormone and an absence of progesterin. Such findings would tend to strengthen Dr. Novak's theory. This would be against the explanation of "mittelschmerz," given by many authorities, namely that it is due to the mechanism of ovulation.

It is interesting to speculate also upon the rôle of the anterior pituitary in the production of dysmenorrhea. May it be that excess follicular activity inhibits the action of the anterior pituitary, preventing its elaboration of Prolan B, the hormone responsible for luteinization and the production of progesterin, the inhibitor of uterine contractility?

We are also faced with this question; why is it that in cases of functional menorrhagia associated with endometrial hyperplasia (in which there is an excess of follicular activity and an absence of the progesterin factor) dysmenorrhea is not an usual accompaniment? In our experience it has been very infrequent.

DR. FLOYD E. KEENE.—If I understood Dr. Novak correctly, he stated that certain experimental evidence has been brought forward indicating that functional

bleeding is of pituitary and not of ovarian origin, as proved by the fact that pituitary implantation following castration and hypophysectomy brought about bleeding. If this be the case, why is it that functional bleeding is cured by ovarian irradiation?

DR. EDWARD A. SCHUMANN.—It has been proved to the satisfaction of everyone but myself that folliculation of the ovary is stimulated by the anterior pituitary. We have just been informed that the ovary remains inert in the body of the female child until the period of the adolescence when it is suddenly thrown into activity by a pituitary hormone. I should like to suggest that the pituitary has also been in the body of the female child for precisely the same length of time as the ovary and the query which at once occurs to me is what stimulates the pituitary to stimulate the ovary at a certain definite epoch in the child's life? Is there still a third energizer of some type or is our conception of this mechanism just a trifle fantastic?

A second point which I should like to emphasize is about the danger of too freely utilizing observations on the lower animal as applicable to the human species. We have just heard of the menstruation of monkeys without ovulation and this observation is frequently showed to explain certain variations in the human cycle. If one will recall the very frequent occurrence of pseudopregnancy in the dog or the invariable presence of two placentas in some of the higher apes when but one young is developed, it becomes obvious that such observations in relation to human functions must be regarded with great care.

DR. NOVAK (concluding).—Dr. Hirst discussed the question of menstruation following presumably complete removal of the ovaries. The case mentioned by him is similar to one reported many years ago by Doran, who likewise was honest enough to re-report his patient later as having been delivered of a child at term. The commonly accepted explanation in all such cases has been that the ovaries had been incompletely removed or that supernumerary ovarian tissue is present somewhere in the pelvis. The fact that monkeys may menstruate without any sign of ovarian tissue makes one wonder whether the occasional persistence of menstruation after apparently complete castration may not be due to some extraovarian factor, possibly hypophyseal, assuming a vicarious rôle in thus maintaining periodicity. Certainly the common effect of castration is cessation of menstruation, so that such a compensatory process must be exceedingly rare, if, indeed, it ever occurs.

Dr. Mazer's skepticism concerning the significance of this latter work I do not think is justified. For example, Dr. Hartman tells me that at present he has in his laboratory four castrated and hypophysectomized monkeys which are bleeding following anterior pituitary injections, although large amounts of theelin in such monkeys cause no bleeding response. He seems also to think that folliculin is responsible for all the changes of the menstrual cycle, merely because it is found even in the corpus luteum, and that the follicle hormone content is high before menstruation. This view is contrary to the best work on the subject. For example, Corner and Allen have shown quite clearly that only progesterin can produce the changes characterizing the pregravid phase, and only progesterin can substitute for the corpus luteum in its important rôle of protecting the nidation of the embryo in early pregnancy.

Dr. Hoffman mentioned a point which I wish he had omitted, in referring to the absence of pain in cases of functional bleeding, where an excess of folliculin is present. This has caused us considerable worry, but Dr. Reynolds, who is still working on the problem, believes that he will soon be able to offer a satisfactory physiologic explanation.

I agree with Dr. Schumann as to the caution necessary in applying to the human being the results of observations upon the lower animals. The rule that folliculin is a stimulator and progesterin an inhibitor of rhythmic uterine contractions appears, however, to be a general one, and even in the human being there has been sufficient work done to indicate that this rule applies in the human female. The phenomenon



which he describes in the case of dogs is evidently the well-known one of pseudo-pregnancy.

Dr. Keene's point as to the mechanism involved in the abolition of functional bleeding by ovarian radiation is well taken, in view of our belief that the bleeding factor is of pituitary origin. We can only speculate as to the explanation. While the sex hormones of the pituitary produce their genital effects only through the agency of the ovary, this does not apply to the bleeding factor, if the work of Hartman, Firor and Geiling is correct. Perhaps the destruction of ovarian function by radiotherapy, with the inevitable secondary atrophy of the endometrium, renders the latter incapable of responding to the pituitary substance.

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## CHICAGO GYNECOLOGICAL SOCIETY

*MEETING OF NOVEMBER 20, 1931*

### **DR. J. B. DELEE presented a specimen of Velamentous Insertion of the Cord.**

This specimen is of great embryologic and of some practical interest. A primipara, about twenty-four years of age, at term, had a little high blood pressure and a little edema of the feet but not enough to cause any concern. She went into labor, with rupture of the membranes, and had complete dilatation twelve hours later. The baby's heart sounds were irregular, slow, and normal. The head came down on the perineum, occiput right anterior, and everything pointed to an easy labor with episiotomy, but her strength gave out, and we did a low forceps. The forceps itself was not difficult, but it was complicated with a great deal of hemorrhage from the perineum. We had to hurry delivery because we could not pack. The baby was quite asphyxiated and required resuscitation. It is now well.

I have seen quite a few of these velamentous insertions of the cord. They are not common. The opening in the membranes was between two vessels, one of moderate size and one enormous, one that ran down the whole length of the opening, through which the baby came.

### **DR. CARL P. BAUER AND DR. CARL W. APFELBACH reported a case of Sudden Death in Pregnancy Due to Rupture of an Aneurysm of the Splenic Artery.**

This patient, eight months pregnant, twenty-four years old, came into the Presbyterian Hospital on August 17. No noteworthy pathology was found during examination. That evening she went home and had some slight pain in the epigastrium. The pain became worse as the evening went on and finally she entered the hospital at 2:00 A.M. She was pale but not excessively so, being more cyanotic than pale. She complained of terrific epigastric pain. Systolic blood pressure was 63. Red blood count was 2,500,000, hemoglobin 45 per cent and leucocytes 11,000. Examination of the heart and lungs was negative. The uterus was soft, reaching almost to the xiphoid cartilage. The fetus presented by the vertex, the head was not engaged in the pelvis. Heart tones were 50 per minute. Rectal examination revealed the cervix closed, the head floating and no vaginal bleeding. Percussion of the abdomen revealed dullness at the level of the iliac crests and backward. When the patient was tipped on the side this dullness extended to the umbilicus.

About five minutes after this examination she was seized with terrific pain in the abdomen, drew her knees up on the chest, became pale, pulseless, and died. The diagnosis at the time was probably intraabdominal hemorrhage. We did not know

exactly what caused the intraabdominal hemorrhage because the patient was not in labor, and we could not believe that she had a ruptured uterus.

At autopsy the abdominal cavity contained 3700 c.c. of bloody fluid. There was no hemorrhage under the peritoneum of the uterus or its appendages. There was free blood in the great omentum and mesogastrium. In the lesser omentum there was bloody fluid. In the peritoneum, in front of the pancreas, there was a small tear. This portion of the peritoneum bulged forward because of a large blood clot which extended from the diaphragm to the pancreas. In the center of this was an aneurysm of the splenic artery midway between the hilus of the spleen and the gastrohepatic ligament and about 1.0 cm. in diameter. The wall of the sac was less than 1 mm. thick. There was free blood in the wall of the sac. There was no change in the celiac axis. The lining of the abdominal aorta was smooth. Except as mentioned, there was no marked change in the important organs of the body.

On sectioning the wall of the aneurysm and staining with hematoxylin and eosin, there was no noteworthy alteration in the intima and adventitia. There were masses in the media that took a blue stain. The histologic diagnosis was excessive retrogressive change, vacuolization and atrophy of the media of the hepatic and splenic arteries.

We report this case because, first, it is extremely interesting from an obstetric standpoint; second, it is extremely interesting from a pathologic standpoint because of the degeneration of the media limited entirely to branches of the celiac axis. The exact nature of these retrogressive changes has not yet been determined.

**DR. CAREY CULBERTSON reported two cases. (1) Imperforate Hymen; (2) Intraperitoneal Rupture of a Vein on the Surface of a Uterine Fibroid.**

**CASE 1.**—This patient was a colored girl of fifteen who had never menstruated. She had pain in the pelvis and in February, 1931 a doctor incised the imperforate hymen, allowing an escape of blood. In March she did not menstruate until the doctor again incised the hymen. In April and May she did not menstruate. She came to the County Hospital. I discovered that she had an imperforate hymen with a little scar representing the point at which it had been incised. Upon resection of the hymen there was a discharge of about 12 ounces of blood, dark greenish in color.

The reason I report this case is because it is one that had been treated and had closed up twice previously, indicating that the proper treatment of imperforate hymen is to resect it and not incise it. It struck me also as being interesting to note that at operation on June 2 there was an accumulation of 12 ounces of blood. Whether all the blood that had been present prior to that had been removed could be questioned. It has occurred to me that in some of these gynatresias where there is a very large accumulation of blood, it might be that the marked distention of the vaginal or uterine wall would permit a serous transudation, thus adding to the total quantity of fluid content.

**CASE 2.**—A colored woman thirty years old presented a large tumor, apparently a fibroid, distending the abdomen. She gave a history of some gastrointestinal distress previously. She had known that she had a tumor in the lower abdomen for two years which had apparently caused little distress. Her menstrual periods had been of three days' duration, every twenty-eight days, and not profuse in amount. She had no dysmenorrhea. Her previous period was ten days too early. The thing that brought her to the hospital was a sudden pain across the lower abdomen. She had noticed that the abdomen had rapidly increased in size for two or three weeks.

At operation we discovered a huge tumor distending the abdomen. There was a very considerable accumulation of blood. This was not all saved but it was estimated that a pint and a half of dark liquid fluid blood was present about the tumor.

The tubes and ovaries were normal. There was no sign of hemorrhage in the broad ligament and no tubal pregnancy. It was not until after the tumor was removed that we discovered the point where the vein had ruptured crossing over the surface of the tumor anteriorly. The finding is rare in my own experience, and I have seen a great many fibroids of the uterus. It is of further interest to note that the patient had a sudden attack of pain in the lower abdomen, probably coincidental with the hemorrhage. There was no history of trauma.

### DR. CHARLES EDWIN GALLOWAY reported a case of **Chorionepithelioma Following Hydatidiform Mole.**

The patient, R. C. H., aged twenty-three years, married three years, was seen for the first time in September, 1929, with a history of irregular and profuse menstrual flow. There was no anemia. Basal metabolic rate was minus 18. Organotherapy was instituted and carried out for three months with no apparent benefit to the patient. She did not return until June, 1930, when she reported that her last period occurred in April and that she was having a little spotting. She was put to bed and remained there for eighteen days. On July 12 there was a spurt of bleeding. She was taken to the hospital and the following day the uterus was evacuated because she continued to bleed. I could only remove part of the hydatid mole because the bleeding was quite excessive. It was about the size of a three and one-half months' pregnancy. I packed the uterus, put the patient to bed, hoping that maybe I would find on removing the packing that the uterus would evacuate itself. The next day she bled very profusely when the pack was removed. I removed as much of the mole as possible. About 300 c.c. of gum acacia was given intravenously and caused a very severe reaction. She had fever for nine days. Her hemoglobin was 30 per cent, and red blood cells 2,000,000. She left the hospital eighteen days later in apparently good condition, with a hemoglobin of 55 per cent, red cells 3,800,000.

Ten days later my visiting nurse reported that the patient was having some spotting. We brought her to the office and on examination found a round blue tumor mass in the anterior wall of the vagina just to the right of the external meatus of the urethra and a little back of it. I sent her to the hospital with a diagnosis of chorionepithelioma, at least from the gross examination. The next morning I dissected out this mass and sent it to the pathologist, who diagnosed it as a chorionepithelioma. I then did a total hysterectomy and an ovasalpingectomy. The patient had a stormy convalescence. Temperature was 102° for three days, then 100° for four days, and then remained normal. The pathologic report showed that the uterus also contained a small amount of chorionepithelioma in its wall, about 15 mm. in diameter. The abdominal wound was infected but it healed very nicely. She left the hospital in ten days. Hemoglobin was 67 per cent and red cells 3,620,000.

I have examined her every month since and she has made a very good recovery. On the ninth postoperative day we did a rabbit test according to Dr. Schneider's modified Aschheim-Zondek technic. This was positive on the ninth day, at eight weeks it was negative; at four and one-half months it was negative. She was last seen in September of this year. She felt fine except for some hot flashes. She weighed 148 pounds, a gain of three pounds over her original weight. Her general condition was excellent and she had no anemia.

### DR. D. A. HORNER reported a case of **Hypersecretion and Retention of Milk in Breast.**

This patient was a nineteen-year-old primipara seen at the Cook County Hospital. The left breast was painlessly distended to the size of her own head. The milk ducts in the nipple were occluded. No milk could be expressed or pumped from that

breast. The other functioned properly. On the sixth day 1900 c.c. of milk were removed from the breast by aspiration. Three days later the breast assumed the same size that it had at first. Again it was aspirated and 1600 c.c. of milk were removed. The patient left the hospital without permitting further work being done, leaving us uncertain as to the true pathology existing. No case is reported containing as much as two quarts of milk retained in the breast.

DR. W. J. DIECKMANN read a paper on **Blood Volume Changes in Eclampsia**. (Not ready for publication. Abstract follows.)

In normal pregnancy examinations of the blood and urine reveal a marked departure from the normal. The changes of significance are an increase in blood and plasma volume, with resultant or causative changes in hemoglobin, hematocrit, and serum protein. There are also alterations in cholesterol, lipoids, surface tension, etc. These changes are more marked in preeclampsia.

In eclampsia there is a concentration of the blood which may be relative (below the average for that period of pregnancy) or absolute (less than the normal). Alterations in hemoglobin, hematocrit, and serum protein are not proportional. Changes in the protein may be the cause of the marked alterations in blood volume. There is also a tendency in pregnancy for a retention of water and NaCl.

Convulsions cause an acidosis which intensifies the changes in the proteins. The concentration of the blood precedes the convulsions but is, however, increased by them.

Since we do not know the exact cause of eclampsia but do know that these changes, above mentioned, do occur and may be incompatible with life, the treatment instituted should be directed at their relief. This treatment, in brief, is to dilute the blood. This may be done by delivery, venesection, plasmapheresis, intravenous glucose or bicarbonate solutions, hypnotics, sedatives, elimination, etc. If the case is mild almost any type of treatment, provided it is not radical, is efficacious; but if it is severe a combination of these procedures should be used. Coincident with a blood dilution the patient improves clinically, as determined by a diuresis, a lightening of the coma, decrease in the temperature, pulse, etc.

DR. IRVING F. STEIN AND MISS COPE presented a paper entitled: **Further Studies on Trichomonas Vaginalis (Donné)**. (See page 348.)

#### DISCUSSION

DR. H. C. HESSELTINE, Iowa City, Iowa.—In the vaginal flora study by Dr. E. D. Plass, I. H. Borts, and myself, we were unable to find any definite relationship in the occurrence of yeast and the vaginal trichomonads, which agrees with Dr. Stein's observations. May I ask if the essayist employs both anaerobic and aerobic media for bacteria?

Goodall of Montreal recently published a report of cures in 22 patients. He used a 1 per cent picric acid cone daily for seven to eight days in conjunction with cleansing daily douches. Following the next few menstrual periods the same medications were employed for two days. In this group there were only two recurrences. The vaginal mucosa apparently thickens and then desquamates.

I was much interested to find that 70 per cent of 31 recently delivered patients, in whom no vulvar irrigation or pads were used, had vaginal trichomonads present in the lochia. They were more often present between the fifth and twelfth day, and at no time were there symptoms or findings of the condition called trichomonas vaginitis. I believe, and soon expect to demonstrate, that the vaginal trichomads are nonpathogenic, even though they frequently are found in certain vaginal infections.

DR. A. J. KOBAK.—We have made a survey of the incidence of vaginal yeast cultures in all phases of life, from the gynecologic clinic, from the diabetic clinic, the prenatal clinic, in children and in certain control patients from the medical wards and from the psychiatric institute of the Research and Education Hospital. In 23 of these patients we have looked for trichomonas and yeasts. Out of the 23, nine were negative for both. It was interesting to study the remaining 14 patients having both yeast and trichomonas or either one of them. In 4 we found both and in all of these 4 there was the typical vaginal discharge that one so frequently associates with trichomonas. One of these patients, a diabetic, had a typical vaginal discharge such as one sees with trichomonas, and also a positive yeast vaginal culture, as well as a yeast infection between the fingers which was definitely verified by cultures and findings at the dermatologic clinic. In three patients having positive yeast cultures but no trichomonas, two had no leucorrhea; one patient had a small amount of discharge that could be accounted for by associated findings. On the other hand, there were seven in whom we found trichomonas and no yeast, but six of these patients had the typical leucorrhea of trichomonas.

Approaching this problem more or less from a different angle, we found that the trichomonas vaginalis rather than the yeast gives rise to or is associated with the vaginal discharge.

DR. FRED H. FALLS.—We have two patients now whom we have been treating for trichomonas vaginalis. The trichomonas has disappeared. Both of these cases showed gram-positive hemolytic streptococci in the vagina. This seems to be a not uncommon complication in trichomonas infection.

DR. STEIN (closing).—Both anaerobic and aerobic cultures were used.

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## CHICAGO GYNECOLOGICAL SOCIETY

*MEETING OF DECEMBER 18, 1931*

### **DR. J. P. GREENHILL presented a specimen of a Ball Pessary Which Had Been in the Vagina for Thirty Years.**

A sixty-four-year-old woman was admitted to the Cook County Hospital with the complaint of bleeding from the vagina, a yellow purulent discharge, and loss of weight of twenty-five pounds during the last six months. Her past history was negative except for the fact that more than thirty years previously a ball pessary was inserted into the vagina by a midwife for prolapse of the uterus. Before that she had had four children. The menopause occurred ten years after the insertion of the pessary.

Examination showed that the woman had a large wooden ball in the vagina in addition there was a left femoral hernia. The ball could not be removed. Before the patient could be scheduled for operation she developed symptoms of strangulation of the hernia. She was sent to the operating room where the strangulation was released and the hernia repaired. An attempt was made then to remove the pessary from the vagina. The ball was freely movable within the vagina but it could not be removed because the introitus was tight, most likely the result of senile vaginitis. Finally I performed an episiotomy, inserted one finger into the rectum high up beyond the ball and with the aid of a speculum under the symphysis pubis, forced the ball out of the vagina. Examination of the vagina and cervix revealed no abnormalities of the mucous membranes in spite of the thirty years which elapsed since the ball was inserted. The bleeding ceased after the removal of the pessary. This

was a hard, perfectly round, solid, wooden ball which measured almost 8 cm. in diameter.

**DR. W. C. DANFORTH** reported a case of **Carcinoma of the Ovary in a Woman at Term.**

A young woman of twenty-three years was admitted to the hospital in late pregnancy, having been sent in by her physician because the child's head would not enter the pelvis. An x-ray was made which showed the head high above the inlet and pushed to the left. On vaginal examination there was an enormous, irregular, hard tumor mass in the pelvis. The cervix was pushed to the left, the head being inaccessible. The previous history was that two years before, she had a tumor removed from the right ovary, the ovary being removed because the tumor was said to be malignant. She had no definite information on that except that the physician told her afterward that it was malignant.

The baby was delivered by a low cervical section. No retroperitoneal glands or enlarged lymph glands were found. The tumor was removed and sections revealed it to be a medullary carcinoma containing a large percentage of embryonal cells. None the less, the prognosis is distinctly bad, in that the tumor is of the type that grows rapidly.

**DRS. M. J. SUMMERVILLE AND F. H. FALLS** read a paper entitled: **A Critical Study of the Technic and Clinical Value of the Sedimentation Rate in Gynecology.** (For original article see page 389.)

**DISCUSSION**

**DR. H. C. HESSELTINE**, Iowa City, Iowa.—The recent obstetric and gynecologic literature continues to have optimistic reports of this test. In 1927-28, by using the Plass technic, which eliminates the factor of cell volume, I studied about the same number of gynecologic patients. This test was shown to have no diagnostic value but some prognostic value in relationship to morbidity and wound healing.

Since advanced pregnancy, intoxication, advanced malignancy, blood absorption, operative and radiation therapy as well as infection in any place in the body increase the rate, and since cell volume, inorganic anticoagulants, dilutions and other factors alter the sedimentation of the red cells, this test can have at most but limited value.

**DR. IRVING F. STEIN.**—As many of you know, Baer and Reis have been working on the sedimentation test for some time, and the reports from Michael Reese Hospital have not been the same as those reported by Summerville. We found that by using the Linzenmeier technic that the results were very good. I do not believe it is a question of the type of technic, but it must be uniformly employed. We found that when Reis was doing the tests regularly, his results were quite uniform, that he regularly got a rapid rate with acute infections. We believe that the greatest value of the sedimentation test is in the subacute infections or in acute infections that are beginning to subside. When the temperature has dropped, the leucocyte count is low and the patient has little to complain of, the sedimentation test is still rapid. That is true in fibroids complicated by salpingitis. Our experience with that group of cases has taught us that if we obtain a rapid sedimentation rate in spite of other normal factors, we frequently found at operation subacute inflammation with cheesy infiltration of tissue that was very troublesome because of the bleeding and because of the difficulty in suturing. We are more likely to have complications in this type, especially thromboses. If we wait until the sedimentation rate has reached one and one-half hours, we usually have no such complications.

We still use the Linzenmeier technic and we use it routinely in gynecologic admissions. We are still guided by the rapidity of the rate. We have not felt this lack of confidence in its preoperative value, but postoperatively we do not utilize it with the same degree of confidence.

DR. FALLS (closing).—Possibly it may be said that in most of the series reported in which the claim is made that one should not operate when a high sedimentation rate is present, the claim is made without proving its correction by operation. Because the rate is high, these authors do not operate. Our object in this series was to determine whether or not, if one operated when it was contraindicated by the test, serious complications would arise. We were not able to find in the literature, except for the series Schmitz had run and a few shorter series, any reports in which the claim was made that one could operate safely in the presence of a rapid sedimentation rate. We felt that at the Cook County Hospital we had been operating for years with good results without the sedimentation test. Surely in some of those cases there must have been a rapid rate. It is interesting to see by the charts that the postoperative hospital stay was no longer in patients with or without a rapid sedimentation rate. Apparently it is not necessary to keep patients in the hospital and to defer operation until the sedimentation rate comes down, as shown by this series of cases.

### DR. J. P. GREENHILL described his results with the use of **Thymophysin and Weak Pituitary Extract**.

Many publications have appeared on the use of this drug especially in the German literature, but no one has reported a comparative study of pituitary extract and thymophysin. I made a detailed comparative study of these drugs chiefly in patients who were in the first stage of labor and who had weak and irregular pains. Because of these restrictions the number of cases studied was small. The pituitary extract used in these experiments was only one-fourth as strong as the pituitary extracts sold commercially, and the thymophysin had an activity of 60 per cent of the U. S. P. pituitary extract. From an analysis of the effects of these drugs in forty cases the following conclusions were drawn:

1. No preparation containing pituitary substance should ever be given routinely or indiscriminately to shorten labor.

2. No pituitary preparation should be administered in the second stage of labor except on rare occasions.

3. Weak pituitary solution and thymophysin are seldom effective for the induction of labor.

4. Both 25 per cent U. S. P. pituitary extract and thymophysin shorten labor in some cases when administered during the first stage of labor.

5. If these substances are used during the first stage of labor, they should be given *only* for a definite indication, namely, uterine atony, or some urgent reason for shortening labor, and *only* small doses should be given namely, 3 minims or less.

6. The 25 per cent U. S. P. pituitary extract and thymophysin seem to give almost the same clinical results. The claims of Temesvary for the clinical value of thymus extract in combination with pituitary have not been borne out. My clinical studies are therefore in accordance with the laboratory finding of Nelson on this point.

7. The addition of thymus to pituitary extract does not add any factor of safety to the use of pituitary. The clinical use of pituitary depends not upon the preparation used but upon sound clinical judgment, time of administration, dosage and close observance of the behavior of the patient.

8. Occasionally weak pituitary and thymophysin even in small doses may do harm. Both have a tendency to increase the blood pressure, both may result in incomplete relaxation of the uterus between pains and both may produce irregularities in the

fetal heart rate which even if it is temporary may nevertheless result in injury to a baby.

### DISCUSSION

DR. LOUIS RUDOLPH.—Since thymophysin contains pituitrin and no specific proof has been shown that thymus extract modifies pituitrin, we must consider, with Dr. Greenhill, that its action is only that of weak pituitrin. I have demonstrated that the unknown factor in uterine contractions is what controls retraction of the muscle fibers of the upper uterine segment, and it is this factor that must be determined in order to solve the problem of functional dystocia. I agree with Dr. Greenhill that clinically and physiologically, pituitrin is a very dangerous drug and that it is safe only when the fetus is out of the uterus.

DR. CARL P. BAUER.—Last spring I reported a series of cases in which thymophysin was used in the treatment of uterine inertia. In this group of cases we considered only those patients who were in labor a much longer time than is normal. The time allowed was twenty-four hours in the primipara and at least twelve to sixteen hours in the multipara without progress. We took these cases because we felt definitely that if we were to get any result from the use of thymophysin, certainly these were the cases that should benefit. In other words, because the patient starts in labor, has seven or eight hours of poor pains without progress, does not mean that within the next hour the membranes may not rupture or pains become stronger and that labor be terminated within the normal period of time. If uterine tetany occurs from the administration of pituitrin, certainly in these cases one would expect it would be less apt to occur because the patient never had satisfactory pains at any time during labor. We considered this group of six or seven cases, though small, was representative of an obstetric problem. In this group we used thymophysin, with the result that we precipitated two cases of uterine tetany and five cases had to be delivered with midforceps after thymophysin had been given. We feel very much as Greenhill does that thymophysin is not satisfactory in the treatment of uterine inertia and that it has some serious dangers. Although the uterus seems to be inert, it goes into tetany after a small dose of thymophysin. Therefore, we do not believe that thymophysin is helpful in the treatment of uterine inertia, nor do we believe it should be used in the first and second stages.

DR. GREENHILL (closing).—When I discussed Dr. Bauer's paper a year and a half ago, I said that thymophysin had a very restricted field of usefulness. Up to that time I had used the drug in thirty cases. I gave only three drops at a time and obtained satisfactory results. However, I did not check up the 30 patients as closely as I did the 40 which were reported this evening. The present intensive study led me to the same conclusions that I made a year and a half ago, namely, that thymophysin (and also weak pituitary extract) should be used only in selected cases in the first stage of labor, only when a patient has weak and irregular pains and there is no progress in labor and only in three minim doses.

DR. R. A. LIFVENDAHL described **A Sign for the Detection of Small Amounts of Free Blood in the Abdomen.** (See page 394 for original article.)

### DISCUSSION

DR. W. C. DANFORTH.—I was surprised that Dr. Lifvendahl did not consider in his symptoms of intraabdominal bleeding the increased leucocyte count. *Leucocytosis* appears promptly and is a definite indication of recent blood and it disappears rather rapidly as the blood becomes absorbed in the abdomen.

As to shoulder pain, that is frequent. I have seen it now in six cases; three reported some years ago and three since then, one occurring a few months ago. In one of these the pain was sufficiently severe to overshadow other pains. Dr. Lifven-



dahl brought out that the shoulder pain is rather secondary because the pain elsewhere is worse. In this one instance it overshadowed the lower abdominal pain so distinctly that at one time the diagnosis was in doubt.

The Cullen sign is a rare thing. I have seen it only once in a series of 80 or 90 cases.

DR. CAREY CULBERTSON.—This observation is very important. It bears out a belief that it is the presence of blood in the peritoneal cavity that causes pain in ectopic pregnancy. The old idea that the pain is due to rupture of the distended tube does not hold today. Blood will cause pain even when it is on the wrong side of the peritoneum, I mean on the outside. Some years ago I reported a case of hematoma of the sheath of the abdominal rectus muscle. In the literature at that time we found 29 cases in women of extraperitoneal hematoma, nearly all of which were thought to be intraperitoneal disease. If, then, the pain is due to the presence of blood in the peritoneal cavity, it is obvious that shifting the patient will shift the pain; at least, that would be the natural supposition. This is all right as long as the blood is fluid. Sometimes, however, the blood is clotted. In what might be called chronic hematocele, where free blood has been in the pelvis for some time, the blood becomes partially or wholly solidified. Then shifting would not take place. We have seen blood fairly solid and we have seen blood in the pelvis that was entirely sealed off by fibrin deposits, and here there would be no change in the pain with change of posture. Sometimes the amount of blood is very small. I have seen a so-called ruptured ectopic pregnancy where there was not more than one ounce of blood and yet the patient had definite pain and tenderness on examination.

DR. A. F. LASH.—With reference to the referred signs associated with rupture and shock, at the Cook County Hospital in the last five years, where we see from five to twelve ectopics a month, we have seen cases where the women have come to the medical department with so-called acute cholecystitis because of pain in the right upper quadrant. They were observed for two or three days and then suddenly had another acute attack of pain and showed evidence of acute intraperitoneal hemorrhage, and only then was the diagnosis made. In another case where the patient had acute pain in the left upper quadrant, it was thought that she had an acute pleurisy. Later she was operated upon for fibroids of the uterus. Free blood was found and an ectopic pregnancy to explain it.

DR. LIFVENDAHL (closing).—I do not believe I shall change my title in accordance with Dr. Lash's suggestion. I said that I had seen one patient early in the morning and laparotomy was done five hours after I had seen her. The test was applicable when the patient was first seen, not after there had been time for extensive hemorrhage. In the second case laparotomy was done nearly sixteen hours after the sign had been observed. The sign is not based upon an abdomen full of blood but upon a small amount of free blood and this constitutes its usefulness in the early stages of intraabdominal hemorrhage and in these only, the very cases in which the other signs are inadequate.

Dr. Danforth brought up the laboratory aspect of extrauterine pregnancy, namely, the leucocyte count. My paper simply dealt with a clinical sign. It is not always possible to resort to laboratory measures unless the patient is in the hospital. I advised the last patient to enter the hospital as soon as possible, since I had diagnosed a ruptured corpus hemorrhagicum. When she came in it was quite obvious that she had an abdomen full of blood and even a blood count was not necessary. The early sign was the guide. Usually, after the patient has entered the hospital, as Dr. Danforth mentioned, the sign is of no value, for frequently the patient is exsanguinated. It is on seeing the patient early, where there is a small amount of blood, that the sign is of value so as to get the patient into the hospital as soon as possible and have her operated upon before she becomes exsanguinated.

# Department of Book Reviews

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CONDUCTED BY ROBERT T. FRANK, M.D., NEW YORK

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## REVIEW OF NEW BOOKS

### MARRIAGE AND ITS PROBLEMS

A number of valuable and informative books have appeared which deal with sex and marriage problems. Careful studies based upon observation, statistics and experience promise to cast an entirely new aspect and afford enlightenment on these obscure and neglected medical issues. The frankness and dignified tone found throughout show that a new and high class of investigators have enlisted in these studies.

In the series of *Medical Aspects of Human Fertility* issued by the National Committee on Maternal Health, Dickinson and Bryant have published an illustrated manual on the *Control of Conception*.<sup>1</sup> This volume is exactly what it claims to be, a short and yet complete manual in which both the general practitioner and the specialist can find definite information and definite guidance upon every aspect of the subject. It covers not only the anatomy, physiology and chemistry involved, as well as the organization and service connected with contraceptive clinics—of which, by the way, the number rose from 28 in 1928 to 80 in 1931, but also the legal status of contraception and sterilization throughout the United States.

Dickinson emphasizes that "birth control is self control." A short and at the same time beautifully illustrated description of the anatomy of the male and female is given; which alone would make the book worth while. The chemical studies of contraceptives is fundamental and informative.

Every contraceptive measure that has ever been advocated is described. Particular attention is paid to the pessaries and intrauterine devices. Such measures as heat applied to the testis in order to produce temporary male sterility are discussed. In the chapter on sterilization without unsexing, vasectomy, salpingectomy and cautery, stricture of the uterine ends of the tubes are considered. This latter measure has been employed in 65 cases.

Therapeutic abortion is analyzed from every point of view, particular emphasis being placed on the medical indications for abortion, sterilization and contraception.

Clinic administration and plans for physicians will be useful to individuals or organizations contemplating the initiation of such clinics, which may include the study of sterility, of birth control, and marriage advice.

This manual is admirable from every aspect. Its general high tone, its utter frankness and straightforward point of view, the clear and concise text, and the beautiful illustrations make it unique in its class.

—R. T. Frank

*Sex Hostility in Marriage* by Van de Velde<sup>2</sup> is a book well worth reading by physicians as well as the highest class of laity. The writer has an exceptional gift in presenting the large and varied material attractively. The book contains a fund of information and the author's personal views with which many will, however, not agree.

In the main he emphasizes a primary sexual antagonism between male and female,

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<sup>1</sup>*Control of Conception. An Illustrated Medical Manual.* By R. L. Dickinson and L. S. Bryant. The Williams & Wilkins Co., Baltimore, 1931.

<sup>2</sup>*Sex Hostility in Marriage. Its Origin, Prevention and Treatment.* Th. H. Van de Velde. Translated from the German by Hamilton Marr. Covici-Friede, New York, 1931.

and additionally a secondary sexual antagonism which consists in a reversal of the impulses of sexual attraction, and consists in a fear of succumbing to this attraction. This is mainly manifested in the female, who is influenced by temporary moods, upon which will largely depend whether the impression is one of attraction or repulsion. In man kinetic energy is the mainspring, in woman it is more a potential energy. Throughout he emphasizes the analogy between the motile sperma and the ovum. With this concept few biologists will agree.

In the male the "will to power" is a motive force, the desire for sexual supremacy and the struggle for existence. Consequently the male is egocentric and solitary, perforce lonely, and hence readily turns to woman for companionship. The woman, on the other hand, the emotional capacity is the main theme and the matter of the moment absorbs her whole interest. In her, tact, intuition, suggestibility, well developed desire for variety are in evidence. If this desire for variety is balked, boredom results. Woman shows vulnerability and plasticity. If these qualities are not duly considered, resentment develops and this resentment may be utilized to attain practical ends by such routes as ill health and hysteria.

As the result of her characteristic sexual qualities, woman has depended on man for protection and support. Dependence is always connected with submission. For these reasons the will to power in woman is inclined to reversal, with consequent desire for subordination and submission to man. She desires submission with her whole soul but seeks to gain power nevertheless. This is the beginning of the struggle and complex.

Work is to man what maternity is to woman. The balked maternal instinct is seen in the childless. Other causes for antagonism are homosexuality, frigidity, etc. "Married hostility is mainly determined by three groups of factors, the specifically sexual, the particular problems of marriage, and the nonspecific problems that also arise." In the portions of the book devoted to prevention and treatment, the choice of partners, parental, intuitive, love choice, choice due to external circumstances are taken up. Such possible sources of dissidence as different desires in work, in pleasures, differences in race, religion, social classes, families, are discussed. The health question governing choice includes sterility, infantilism, infection. Among character conditions, hormonal constitution is discussed. Great emphasis is given to Kretschmer's classification into cyclothymic and schizothymic. By preference, partners should select opposite types, the pyenic-cyclothymic mating with the schizothymic leptosome.

How many serious minded physicians will agree with the importance attached to character reading by means of graphology, I will not try to answer.

A frequent source of trouble often results from putting marriage below the importance of parents or children. Trouble is caused by ineffective erotic training. The author is convinced that biologically there are two standards but he warns man against taking advantage of this. All medical men will agree that gynecologists should not neglect psychotherapy. He adheres neither to Freud's nor Adler's theories and warns against overrating either. The "Marriage Doctor" should be an old broad-minded gynecologist. In his day, the old family physician filled this rôle to a surprising degree.

From this brief résumé, the amount and broadness of the material dealt with can be readily appreciated. Many will disagree with the beliefs of Van de Velde but no one can fail to appreciate the great value of this book which is the second in the trilogy of which the first was "Ideal Marriage."  
—R. T. Frank

Van de Velde finishes his trilogy on marital problems with this volume.<sup>3</sup> The three books *Ideal Marriage*, *Sex Hostility in Marriage* and the treatise in hand

<sup>3</sup>**Fertility and Sterility in Marriage. Their Voluntary Promotion and Limitation.** By Th. H. Van de Velde, M.D. Translated by F. W. Stella Browne and C. A. Bang. Covici-Friede, New York, 1931.

cover in a comprehensive manner what may be called the marriage problems of the present age.

Here he discusses fertility and sterility. The introductory chapters consider both subjects from an ethical and theologic standpoint. The latter contains direct references to the church laws of various denominations as they relate to certain medical situations. Then follows a broad philosophical discussion on fertility as it affects the individual and the state, the ethnic and international aspects of family limitation.

Sterility in male and female is considered from both physiologic and pathologic angles. Van de Velde does not feel that glandular, hormone, treatment or surgery offers much in female sterility. There is a short chapter on artificial insemination.

In the final section of the book practically all the known methods of preventing conception are considered at length. Van de Velde discusses an operation of his own, encapsulation of the ovaries, in a consideration of the methods of temporary sterilization. He abhors the practice of abortion and states his personal views on the subject.

This series of books is a thorough and seriously minded dissertation on the complexities of married life. Van de Velde is not a propagandist of birth control, he recognizes it as a problem of present day life and discusses it in its sociomedical relations. Similarly he has considered the intimate psychical and physical relationships of marriage and the significance and therapy of infertility.

—Philip F. Williams

The practice of contraception<sup>4</sup> as a world problem has attained the age and dignity of a Seventh International Conference. The earnestness and scope of the work in this field is revealed by the character of the papers read and the number of different countries represented in the discussion. While many methods were described the most widely accepted method seems to be a mechanical occlusive device either alone or in conjunction with a chemical paste or jelly. The uncertainty of intra-uterine devices and the dangerous effects of cervical appliances are evident from the reports presented.

Of particular interest is a section of biological methods, illustrated by a paper on "Hormonic Control of Fertility" by Taylor of Edinburgh. This paper is extremely suggestive of the many previously hidden bypaths of endocrinology opened up by the research work of the past few years. While this method, as well as the use of spermatoxins, is still in an experimental state, the results obtained from animal experimentation promise much. Sterilization, both male and female, was considered, but methods are not discussed. It is remarkable that so much space has been given to the interruption of pregnancy, two methods for abortion being described in considerable detail. One method, the intrauterine injection of a paste, the action of which is shown in some excellent uterograms, was invented by a German pharmacist who applied it in 11,000 cases, ceasing his labor apparently because he was sentenced to three years' imprisonment for aborticide. The roentgen ray technic for abortion is brought up only in the discussion. Van de Velde, the chairman at this meeting, regrets the introduction of the technic of induced abortion, feeling that it is out of place in a symposium on the control of conception; a point very well taken.

The remaining chapters of the book describe the extent and methods and spread of birth control propaganda in various countries. The legality of the practice varies greatly. The social significance of contraception seems to have permeated deeply into such overpopulated nations as China and Japan. What future effect this may have on world economics and politics is speculative.

—Philip F. Williams

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<sup>4</sup>**The Practice of Contraception, an International Symposium and Survey.** Edited by Margaret Sanger and Hannah M. Stone, M.D., with a Foreword by Robert L. Dickinson, M.D. From *The Proceedings of The Seventh International Birth Control Conference*, Zurich, Switzerland, September, 1930. The Williams & Wilkins Company, Baltimore, 1931.

Exner has succeeded to a remarkable degree in dealing with the sexual side of marriage<sup>5</sup> in an honest, informative and irrefragable fashion. It is a successful attempt by a medical man to present the subject to the laity in a fashion to point out the way "to marriage at its best." The book is designed for men and women approaching the marriageable age and for married couples in whom maladjustment has developed. Its appeal is to the intellectually mature.

A few quotations may illustrate the contents. "Harmony and mutual satisfaction in the sexual sphere is likely to be the sustaining vital breath of the marriage as a whole." "We have seen now that in nature the primary biologic function of sexual union is the continuance of the species. The keen pleasure premium associated with it arose as a byproduct, as it were." "So out of this primitive physical attraction between male and female, serving primarily biologic ends, there has been woven strand by strand the marvelous pattern of human sympathy, affection and love which so greatly enriches the life of man and which underlies the structure of our social life."

The anatomy of the male and female sex organs is thoroughly but discretely described without inhibitions but without indiscretions, and is well illustrated by diagrams from Dickinson.

In summarizing the sex differences the author states that "In men sex desire is fairly uniform; it lies close to the surface and is easily aroused and quickly satisfied, and man is always liable to sex desire in all its forms. In women sex desire is variable; it lies deeper and is more slowly aroused and more slowly satisfied; it is subject in most women to tidal rhythm; and it is subject to development to full power through experience. In the next chapter we shall discuss more fully the adjustment problems that arise out of these differences and out of ignorance of them."

The sex factors in maladjustments are entered into in great detail and with good judgment. Such subjects as sex technic, difficulties and their cure, frigidity, dyspareunia, fear, the rôle of contraception are entered into.

The next chapter deals with ideal marriage, including the ideal itself, the choice of mate, health, compatibility, tastes and desires, harmony, etc. Engagement, premarital examination, premarital knowledge, initiation are discussed. The concluding chapter deals with the family. All in all this is an admirable book to be highly recommended with the reservation that it should be limited to those qualified by education and maturity to appreciate its full value.

—R. T. Frank

Dr. Evans states that the particular reason he had for undertaking to write this book<sup>6</sup> was to call the attention of unseeing husbands to the frequent unsatisfaction of the wife in the marriage relation. In a simple common-sense manner the intimate problems of marital adjustment and the solutions of maladjustments are described. The book is refreshing in the difference it exhibits from the usual sex and marriage publications. The frank, yet delicate, handling of the subject makes the manual one that a physician may safely suggest, when necessary, to his women patients, and it would harm no husband to be acquainted with the contents of this book.

—Philip F. Williams

#### GYNECOLOGY

Halban's *Gynecological Operations*<sup>7</sup> is a very valuable contribution to gynecologic surgery. Its value is enhanced by the fact that the author has emphasized the technics which are generally accepted and has not hesitated to stress his own views.

<sup>5</sup>The Sexual Side of Marriage. M. J. Exner. W. W. Norton & Co., Inc., New York, 1932.

<sup>6</sup>Man and Woman in Marriage. Dr. C. B. S. Evans, With an Introduction by Dr. Rudolph Wieser Holmes. Bruce-Roberts, Inc., Chicago, 1931.

<sup>7</sup>Gynäkologische Operationslehre. von Hofrat Prof. Dr. Josef Halban. Urban & Schwarzenberg, Berlin, 1932.

The vaginal method which he regrets that the younger gynecologists have largely abandoned, is particularly stressed.

As an anesthetic, Halban prefers general or local anesthesia, using spinal anesthesia only in exceptional cases. Every gynecologic operation is described in detail. For example the transplantation of the vestibulo and vaginal anus into the normal location is fully described and well illustrated. In the treatment of uterine displacement, a considerable number of operations are advocated, including ventrofixation, vagino- and vesico-fixation, Alexander's operation, and various other technics for shortening of the round ligament. Shortening of the sacrouterine ligaments is likewise advocated. Personally he prefers high vesicofixation, either abdominally or per vaginam. This preference is based on almost 100 per cent of success. The Alexander-Adams operation is reserved for cases in which an inguinal hernia is present.

In the treatment of prolapse, Halban's views should be considered with a great deal of attention because of his well-known anatomical studies of prolapse in conjunction with Tandler. Throughout the book his viewpoint is extremely conservative, insisting that minor conditions require no intervention unless symptoms develop. In his description of the operation for complete prolapse, he describes a technic as his own, which, except in minor details, corresponds exactly to the Fothergill operation so generally practiced in Great Britain. This operation is based upon high amputation of the cervix with exposure of the area harboring pubocervical tissues and base of the parametria. He is strongly opposed to vaginal hysterectomy and prolapse but if one can judge from the text, has not informed himself of the advances recorded in the United States and Canada in this technic.

The chapter dealing with carcinoma of the cervix is of great interest, containing as it does a very excellent summary of the world's results, both by abdominal, vaginal, and radiotherapeutic measures. He has to his credit a large series of cases in which either abdominal or vaginal hysterectomy was performed and apparently the results by the two methods were approximately identical. Consequently he prefers the vaginal route which entails less risk to the patient. His operative technic does not appear to me as radical as that described by v. Peham and Amreich. In his hands radical vaginal hysterectomy takes only fifteen to twenty minutes.

For sterility accompanied by dysmenorrhea, he advocates discission and curettage, and likewise, to my surprise, considers curettage in amenorrhea a powerful stimulus to ovarian function. Temporary sterilization in some cases is obtained by placing the osteal end of the tubes anterior to the uterus, into the vesicovaginal space.

The text concludes with the discussion of operative correction of ventral and other hernia, vesicovaginal fistula, approach to the ureter and kidney.

The author describes and illustrates the Trendelenburg operation of embolectomy although he mentions A. W. Meyer's technic. The latter technic appears so superior that it would have been preferable to illustrate this modification rather than the original Trendelenburg operation in which the pleura is opened. I cannot agree with Halban's statement that skin methods for the establishment of an artificial vagina are useless as they have proved extremely satisfactory in my hands and unaccompanied by the risk of intestinal transection.

The illustrations of this book are excellent, simple, but artistic, and fully illustrate the text. In fact, the entire book can be most highly recommended to the profession because of its simplicity, conservatism and simplification of technic.

—R. T. Frank

Hertzler has published *Surgical Pathology of the Female Generative Organs*<sup>s</sup> in which he professedly mentions only "the things that he has seen" and the end-results of what he knows. Although this book is somewhat sketchy, it contains a large

<sup>s</sup>*Surgical Pathology of the Female Generative Organs.* Arthur E. Hertzler. J. B. Lippincott Co., Philadelphia, 1932.

fund of useful information, presented in a striking and readily assimilable form. The entire field of gynecologic pathology is covered in surprisingly short compass. Naturally this entails many omissions which however will not be missed by the student or the occasional operator who desires readily obtained information. The author abhors theory and complication to a marked degree, and throughout stresses a common-sense point of view which is admirable.

The bibliographies with short notes at the end of the chapters are very useful. These bibliographies could have been improved by making the names of the authors stand out in different type.

All experienced gynecologists must be in hearty accord with the quotation "the ovary has been the most mistreated of all organs" and the advice that, as Hertzler puts it "involutional states of the ovary" in which he includes atresia, polycystic ovaries, perioophoritis, are not to be regarded pathologic or diseased, and require no intervention.

It might have been brought out that bartholinian cysts are almost always cysts of the duct and not of the gland proper. Few will agree that pruritus is due to a discharge "the product of aging cervical glands." Carcinoma of the clitoris, in my experience, has not been either of slow growth or of good prognosis, as Hertzler mentions, nor can I agree that sarcoma of the ovary and teratoma of this organ are more or less identical.

The illustrations of this book are admirable and instructive. This applies both to those showing gross lesions as well as microscopic specimens. —*R. T. Frank*

This excellent manual on operative technic in gynecology<sup>9</sup> is a companion volume to the volume on surgical technic of the biliary passages. The introduction is written by M. Robineau and W. Stern.

The subject matter is systematically arranged with each operative step accurately described and profusely illustrated. Like most texts the first chapter deals with the general preparation of the patient, the anesthetic, the position of the patient and the incision for celiotomy. The author employs the routine low median incision in preference to the Pfannenstiel or transverse incision. We do not concur in the view that the Pfannenstiel incision offers the difficulties indicated by the author, nor that the time in the menstrual cycle is an important factor. The chapter on postoperative celiotomy is well written and considers the more common complications encountered.

All the classical and time tried operative procedures are described and profusely illustrated with a clarity that is characteristic of most French writings.

This text book will occupy an important place in gynecologic technic and serves its purpose in a most admirable way.

—*Sydney S. Schocket and Julius E. Lackner*

Döderlein<sup>10</sup> has given a short presentation of inflammatory diseases of the female pelvic organs which is given in a conservative and attractive fashion. I cannot agree with the advice to obtain spreads from the uterine cavity in gonorrhea, as this favors infection of the adnexa. On the whole this book is well gotten up.

—*R. T. Frank*

Dr. Forsdike has written a small text on gynecology<sup>11</sup> for use of students and practitioners, which compares favorably with some recent manuals of a similar nature appearing in this country. The material covers all the subject of gynecology

<sup>9</sup>*La Tactique Operatoire des Annexes de L'Uterus.* By Raoul Charles-Monod. Publiee Sous La Direction de M. Robineau et W. Stern. Published by G. Doin & Cie. Paris, France.

<sup>10</sup>*Die konservative Behandlung entzündlicher Genitalerkrankungen der Frau. (Therapie in Einzeldarstellungen.)* Priv.-Doz. Dr. Gustav Döderlein. Georg Thieme, Verlag, Leipzig, 1932.

<sup>11</sup>*Textbook on Gynaecology.* By Sidney Forsdike. William Heinemann, Ltd., London, 1932.

briefly yet thoroughly. Many of the illustrations of specimens have been drawn from the recent Cuthbert Lockyer collection, an indication that this superb collection of gynecologic material is going to be made use of. The section on radium is especially good, a few minor criticisms might be made here and there; a dissenting opinion might be expressed to the statement that a gas pressure of 300 mm. Hg is permissible for a Rubin test. Similarly one is surprised to find a description of five types of endometritis.

—Philip F. Williams

Professor Strassmann<sup>12</sup> presents the medical and dietetic treatment given his patients. This edition is thumb indexed and has been printed in booklet form at the request of students and physicians.

This edition differs from previous editions in that it includes points in diagnostic and social hygiene. This outline was never meant to be a scientific treatise, but rather a collection of practical points from the experience of the author on diagnosis and treatment from the gynecic point of view.

—Sydney S. Schochet and Julius E. Lackner

Sellheim's *Wechseljahre der Frau*<sup>13</sup> is a brochure composed largely of a critique of Dr. Helene Friederike Stelzner's book on the climacteric. He does not agree that the symptoms of the menopause need be excessive but feels that she is correct in assuming that women have greatly exaggerated the fear of the change of life.

—R. T. Frank

The twelve articles contained in this collection<sup>14</sup> are from the Gynecological Clinic of Copenhagen, directed by Prof. Gammeltoft, and have appeared in various journals. Seventy per cent of them are in German, French and English, the rest in Scandinavian.

Brandstrup discusses the significance of gonorrhea in the puerperium. Of 2000 patients, 13 per cent gave a serologically positive gonorrheal reaction. The morbidity among these was 33 per cent while among the nongonorrheal patients only 18 per cent morbidity was observed postpartum.

Damm considered esthiomène a symptom-complex arising when the regional lymphatics are choked. Drucker treated 49 children in bad tuberculous surroundings per orally with Calmettes B.C.G. with good results. The longest article is by Nielsen, dealing with clinical studies of tuberculous salpingo-oophoritis and its prognosis. This article is 282 pages long and in Danish. The volume concludes with the statistics of Rigs Hospital for 1930 and 1931. This is the seventh volume of the series.

—R. T. Frank

There is a definite need for this excellent text book<sup>15</sup> on gynecology and urology. The scheme of outline of including urology with gynecology is a departure from the traditional grouping of this subject with obstetrics. The arrangement of the subject matter and the illustrations are well executed except for a few minor typographical errors. The newer proved methods of diagnosis and the adjuncts in gynecology are properly evaluated. The author fails to emphasize the more important symptoms that should indicate the presence of complications to the nurse. The chapter on postoperative care appears to be the routine hospital rules rather than a discussion of treatment.

<sup>12</sup>*Arznei-diatetische, diagnostische und sozial-hygienische Verordnungen für gynäkologisch-geburtshilfliche Praxis.* By Paul Strassmann. Ed. 5. Published by Georg Thieme, Leipzig.

<sup>13</sup>*Wechseljahre der Frau. Ihre Bedeutung für das Leben.* von Geh.-Rat. Prof. Dr. Hugo Sellheim. Ferdinand Enke Verlag, Stuttgart, 1932.

<sup>14</sup>*Arbejder Fra Fødenafdeling A Og Gynaekologisk Afdeling. Rigshospitalet.* VII Bind. Udgivet af S. A. Gammeltoft. Levin & Munksgaard, København. 1932.

<sup>15</sup>*Gynecology and Urology for Nurses.* Samuel S. Rosenfeld. pp. 230, New York, William Wood & Company.



The text is clearly written without frills, neither too elementary nor too involved, and illustrated with plates from standard text books. On the whole this booklet is well above the average.

—*Sydney S. Schochet and Julius E. Lackner*

#### OBSTETRICS: FETUS AND NEWBORN

Goodall's *Puerperal Infection*<sup>16</sup> although designed for the senior medical student and general practitioner, may be read with pleasure and profit by the specialist, because of its judicious viewpoint, clear and pleasant method of presentation, and an unusual combination of simplicity and thoroughness.

Full justice is done to the Manchester school, especially White and Kirkland who as early as 1773 clearly understood the causation of puerperal sepsis, followed in 1826 by Collins of Dublin, in 1843 by our own Holmes, in 1850 by Semmelweis. The essentials of bacteriology are presented. The unreliability of mortality statistics is emphasized. The main agents for infection are the accoucheur and more rarely the husband.

The author takes a middle standpoint between those who advocate vaginal or rectal examinations exclusively. He ascribes delayed involution mainly to cervical infection. His standpoint as to treatment is strictly conservative and places no reliance on vaccines or antiserum. Although the value of the protein reaction is considerable in chronic conditions, he justly decries its use during the acute inflammatory stage. Goodall's personal experience in transfusion is limited to the citrate method. He warns of the danger of transfusion at a critical stage of the disease although a firm believer in its therapeutic value. The book is admirably conceived and well written.

—*R. T. Frank*

Experience during the past years have shown us the value of abdominal cesarean section and its place in future obstetrics.<sup>17</sup> The author discusses the modern indications of cesarean section and bases his point of view on his extensive clinical experience, the critical study of the literature over a period of years, and the experiences of Professor Wieloch of the Universitäts Frauenklinik in Königsberg.

Previous to 1928 there were only three or four indisputable indications for cesarean section. Since 1928 the literature shows that the abdominal cesarean section has been performed for 63 different indications, many of which have not received recognition by obstetricians of the world.

Binthen in Halban-Seitz *Biology and Pathology of Obstetrics* outlines the various indications. The author attempts to collect and discuss critically 3000 cases of cesarean section.

The indications are grouped under six subdivisions:

- (1) Disproportion between child and birth canal.
- (2) Immediate termination of pregnancy in the interest of the mother.
- (3) Immediate termination of pregnancy in the interest of the child.
- (4) Replacement of the vaginal method of delivery in placenta previa, transverse presentation and lack of engagement.
- (5) Termination of pregnancy in the last months of gestation on account of heart disease, lesions of the kidneys, post maturity of the fetus and tuberculosis of the lungs.

(6) Obstruction of the vaginal canal due to diseases of the vulva, vagina, varicosities and infectious processes.

This book is well written and presents a clear and concise discussion of cesarean section. While we hesitate to criticize Professor Winter's list of indications, we feel

<sup>16</sup>*Puerperal Infection*. James Robert Goodall, (printed privately), Montreal, 1932.

<sup>17</sup>*Die Indikationen zum Abdominellen Kaiserschnitt für alle Kaiserschnitt-Operationen*. von Professor Dr. George Winter, 1931. Published by Ferdinand Enke, Stuttgart.

that there are too many cesarean sections performed without rigid indications. We should remember that maternal mortality of cesarean section is more than five per cent.

—*Sydney S. Schochet and Julius E. Lackner*

The author analyzes<sup>18</sup> 352 consecutive cases of cesarean section which have been personally operated on from 1919 to 1930. A brief historical survey of cesarean sections contrasting the published records of the comparative value of the classical and low cervical sections is given. In the cases reported there is a mortality of 7 or 1.9 per cent, which must be considered excellent, as all types of cases are included. No craniotomy on a living child was performed on the author's service during the period of review, nor was there a hysterectomy on any case following cesarean except for fibroid tumors. Of the 99 sections which were repeat operations there was one fatality. On 2 occasions a definite aperture was found in the scar. Two cases of the 352 were known to have ruptured in subsequent pregnancies with fatal results. Chronic nephritis or syphilis, or both together, are considered to make the prospect of sound healing of the wound very remote and sterilization is suggested in such cases.

The author feels the problem in cesarean work to be improvement of the technic so that the potentially infected case may be operated upon with a risk as low as, or lower than, craniotomy. The low classical method was used, the uterus was even-trated, interrupted sutures inserted, antistreptococcus serum given at the time of the operation, and drainage used almost routinely. No attempt is made to sterilize the vagina. In making the incision care was taken not to encroach upon the lower uterine segment where bleeding is more difficult to control. Saline is used freely and in no case was a transfusion considered necessary or advisable. In clean cases the drainage tube and serum administration were often omitted.

In the sections for contracted pelves, early in labor, the mortality rate was 1.2 per cent; in the 66 cases operated upon late in labor, while the morbidity rate was 50 per cent, there was only 1 fatality. Comparisons between the suggested low classical and the cervical section are brought up frequently. The author is averse to the latter on account of the technical difficulties and complications and feels that the technic is more easily performed by the occasional operator, and one must agree that excellent results were secured in achieving a maternal mortality of 2 per cent in a large series of mixed cases. It is acknowledged that it is too early to make a comparison between the two operations from the standpoint of subsequent rupture of the scar.

A very good review of an always interesting topic.

—*Philip F. Williams*

The fourth edition<sup>19</sup> of this text book is similar in style and contents to its predecessors. The book is a collaboration by ten teachers representing eight medical schools and three large lying-in hospitals. This type of book seems especially popular in Great Britain. With the exception of a few systems of medicine, we have nothing comparable to it in this country. One loses on one hand the fully expressed personal views of a particular author, on the other hand as all the manuscripts are corrected and read by the whole editorial staff one may gain from their collective experience. As the purpose of the book, as expressed in the preface of the first edition, is to prepare students for their final examination, presumably a collective presentation of the subject may better fulfill this aim.

In this volume the newer physiology of ovulation and menstruation is included. The mention of veratrum viride and chloroform in the treatment of eclampsia mars

<sup>18</sup>*Caesarean Section, An Analysis of 352 Consecutive Cases of the Classical Operation, With an Account of the Technique Employed.* By Frances Ivens-Knowles, C.B.E. J. & A. Churchill, London, 1931.

<sup>19</sup>*Midwifery by Ten Teachers, Under the Direction of Comyns Berkeley.* Edited by Comyns Berkeley, J. S. Fairbairn, Clifford White. Fourth Edition. William Wood & Company, New York, 1931.

a good chapter. The contributor on cesarean section feels quite strongly opposed to sterilization, stating that abortion, if a subsequent pregnancy develops, is a less immoral procedure than mutilation of the woman's body. Although two pages are devoted to discussion of sterilization no mention is made of the low cervical section. The proof reading has been faulty, page 363 shows a gross error and the legends of Figures 174 and 175 are transposed.

—Philip F. Williams

The 1930 *Medical Report of the Glasgow Royal Maternity and Women's Hospital*<sup>20</sup> is mainly statistical. Among 4469 admissions, there was a maternal mortality of 2.6 per cent. In the case of emergency admissions it was as high as 4.3 per cent. In this group of admissions, 15 cases of mole were found. The detailed statistics should prove of advantage to obstetricians.

—R. T. Frank

The second edition of Adler's *Care of the Woman*<sup>21</sup> has been expanded, according to the preface, to bring in some new points on physiology, health culture, and the inclusion of some new illustrations. The manual is intended as a text book in nurses' training schools, and, in addition, Adler hopes that it will serve as a manual for personal hygiene in women. The book discusses appropriate topics concerning pregnancy, labor, and the puerperium and the final chapter is on nursing after gynecologic operations. A disproportionate amount of space seems to be devoted to the subject of vaginal douching in pregnancy, but this minor criticism is offset by the excellence of the following section on the preparation made by the nurse or attendant for a delivery. Prophylaxis of puerperal fever is well written. There can be no doubt that the book amply fulfills the purpose for which it was intended.

—Philip F. Williams

This introduction to obstetrics, in its fourth edition,<sup>22</sup> is deserving of popularity. Designed primarily for the student, the important normal features involving the female reproductive system, development of the child, and the mechanism of labor are clearly and concisely presented. The more common abnormalities encountered are touched upon but the normal is stressed. Mensuration is thoroughly described. The biologic diagnosis of pregnancy is gone into at considerable length, much more than is warranted. Some 15 tests are described, 13 of which never could be considered reliable and which in the light of the present-day Aschheim-Zondek and Friedman tests must be relegated to the limbo of medical curiosities. Why the student should be burdened with them is hard to understand.

In this regard, exception must also be taken to mentioning in a work designed as introductory the use of an opaque medium in the uterus for the diagnosis of pregnancy. As to uterosalpingography for diagnosing ectopic gestation one must certainly draw the line. In spite of these manifest superfluities this is a useful book, up to date, and well annotated. The illustrations are adequate. Each chapter is summarized, probably of benefit to the student in retaining the material.

—Frank Spielman

This monograph<sup>23</sup> is on the subject of welfare for childbearing women and is the key of social gynecology. The author has been interested in this work for more than

<sup>20</sup>*Medical Report for the Year 1930. Glasgow Royal Maternity and Women's Hospital.* Prepared by H. R. MacLennan. Aird & Coghill, Ltd., Glasgow, 1931.

<sup>21</sup>*Die Pflege der Frau in der Schwangerschaft, im Wochenbett und bei Frauenkrankheiten.* Von Dr. Ludwig Adler. Zweite Auflage. Franz Deuticke, Leipzig und Wien, 1932.

<sup>22</sup>*Propeudencia Obstetrica.* By Arnaldo de Moraes. (Portuguese.) Fourth Edition. Fred H. Sauer, Rio de Janeiro, Brazil.

<sup>23</sup>*Monographien zur Frauenkunde und konstitutions Forschung Fortsetzung der Monographien zur Frauenkunde, Frauenkunde und Eugenetik, Sexualbiologie und Vererbungslehre.* Herausgegeben von Dr. Max Hirsch, Berlin, Leipzig. Verlag. von Curt Kabitzsch, 1931.

twenty years and answers the many questions on this subject by means of short papers. Abstracts of these various papers have been placed before the Minister of Interior Department of Germany. The German Congress of the Society for Obstetrics and Gynecology empowered Professor Max Hirsch to write on the welfare of women in puerperium.

The treatment of women in puerperium is for the most part empirical when not based on scientific principles. The treatment of women in puerperium is one of the most important branches of health welfare.

The author gives the rules and regulations for establishing welfare stations for childbearing women, pregnant and nonpregnant conditions referred to females from childhood to maturity. Questions are answered as to what to do, when confinements are to take place in institutions and in the home. Detail chapters on welfare of patients following confinements; welfare organizations; open institutions; and closed institutions.

This is a very complete and concise monograph on the subject of the childbearing woman.  
—*Sydney S. Schochet and Julius E. Lackner*

Here is an earnest little book<sup>24</sup> frankly propaganda for the enactment of laws in the new Spanish republic designed to safeguard those who contemplate marriage, as well as any future offspring. The arguments gleaned from an extensive bibliography, although often repeated in the past are incontrovertible, and worthy of universal attention. The author points to numerous countries, among them the United States, which have propagated laws entailing supervision of marriage in some form. It may be called to the author's attention that in most cases these laws even if extant are either not enforced or not enforceable. In these days when much is heard of "personal liberty" any suggestion of apparent further curtailment leaves one apathetic. Nevertheless, the tragedies witnessed by physicians in general, gynecologists in particular, must if thought about make numerous converts to this cause.

—*Frank Spielman*

Dr. Stahl discusses his views on various embryologic subjects.<sup>25</sup> He believes the earliest blood and vascular elements originate in the chorion and its villi, and not, according to divergent theories, in the area vasculosa. There are, also, some remarks on the origin of cancer, with reference to the primal nucleocellule.

The author evidently feels quite keenly the charges of heterodoxy made upon a previous presentation of his views.

—*Philip F. Williams*

Scammon and Calkins have accomplished a gigantic task in their monograph describing the growth and dimensions of the human body in the fetal period.<sup>26</sup>

The authors divide the subject into three periods, that of the ovum, the embryo, and the fetus. Four hundred selected fetuses from 2.3 to 54.4 centimeters are the basis of the study. In each case 71 external measurements have been taken. They use the crown-heel length. Artifacts resulting from formalin fixation, vascular injection, birth moulding, and chest configuration due to the first intake of breath, required consideration. The text proper does not lend itself to a detailed review as it consists largely of an enormous amount of statistical material. The monograph is concluded by a large bibliography. This book will prove of interest to embryologists and obstetricians who can refer to the material as their needs require.

—*R. T. Frank*

<sup>24</sup>*Eugenesia y Matrimonio* (Spanish). By F. Haro Garcia. Javier Morata, Madrid, 1932.

<sup>25</sup>*Concerning the Origin of First Blood Corpusele, First Blood Plasm, First Blood Space, First Blood Vessel. Origin of Cancer.* By Frank A. Stahl. Published personally, printed by Franklin Co., Chicago, 1931.

<sup>26</sup>*Growth in the Fetal Period.* R. E. Scammon and L. A. Calkins. The University of Minnesota Press, Minneapolis, 1929.

In the form both of books and paper bound pamphlets the transactions of this important conference are gradually being published.<sup>27</sup> Investigations, more thorough and more competent than ever before attempted, have brought together a wealth of valuable information for the medical and nursing professions and the social worker.

A critical analysis of undergraduate and graduate *Education in Obstetrics* is presented by two committees, headed by Dr. Palmer Findley and Dr. Rudolph W. Holmes, respectively. Briefly summarized these reports come to the conclusion that more adequate courses should be provided.

Similar in concept as well as in regard to final conclusions is a report on *Pediatric Education* prepared by Dr. Borden S. Veeder.

A volume, entitled *Psychology and Psychiatry in Pediatrics: the Problem*, is presented by a committee under the chairmanship of Dr. Bronson Crothers. "Unwillingness of doctors at large to acquire the ability to deal wisely with problems involving personality of the child," says this report, "may lead to transfer of this field to formal organizations or to individuals without medical experience." All doctors cannot become experts in the fields of psychology and psychiatry, but advice on adequate physical care certainly cannot be given without attention to whatever intellectual or emotional difficulties may be present.

There is a report in book form by a committee headed by Dr. Robert B. Osgood dealing with *Body Mechanics: Education and Practice*. To what extent does poor or good posture affect physical fitness? What constitutes good posture—or body mechanics, a better term used in this connection? What is taught about body mechanics in medical and other schools? How much should be taught and by whom? These are some of the questions fully answered in this volume.

There is another, larger volume of 275 pages, devoted to a consideration of *Health Protection for the Preschool Child*. It represents a national survey of the use of preventive medical and dental service for children under six, made under supervision of George Truman Palmer, Ph.D., Mahew Derryberry and Dr. Philip van Ingen. To assemble the necessary material nearly a thousand different local organizations investigated 146,000 children living in cities, 37,000 living in the open country and small towns. Three-fourths of all cities of over 50,000 population and rural areas in 42 states were included in this survey. The result is a most complete and graphic picture of how preventive medical and dental services are being applied to the young child in this country. That already available knowledge at present is not sufficiently applied might well be deduced from the surprising fact that only one-half of the city children and but one-third of the rural children had the benefit of a health examination, that only 7 per cent of the country children under six years have been vaccinated against smallpox.

Many more reports of this sort will appear in the near future and will be discussed in this department after publication.

—Hugo Ehrenfest

In this monograph<sup>28</sup> of 270 pages the author presents a careful anatomic study of cerebromeningeal lesions of the newborn and discusses their possible later sequelae. He stresses justly the importance of spinal puncture particularly for diagnostic purposes, and the difficulties encountered in the proper interpretation of such findings. In regard to the causation of such lesions he dwells upon certain obstetric mechanical factors but like most French writers seems to exaggerate the etiologic significance of syphilis. Among the 58 illustrations those picturing histologic findings are of noteworthy excellence. This volume necessarily will prove of interest and value both to obstetricians and pediatricians.

—Hugo Ehrenfest

<sup>27</sup>White House Conference on Child Health and Protection. Proceedings, published by The Century Co., New York, 1932.

<sup>28</sup>Les Lésions Cérébro-Meningées à la Naissance. Par Robert Waitz, ancien interne des hôpitaux de Paris. With 58 figures in the text. G. Doin & Cie, éditeurs. Paris, 1931.

In this small volume<sup>22</sup> an obstetrician and a syphilographer have collaborated in a discussion of syphilis as it is found in obstetrical practice. The authors emphasize the importance of the early diagnosis of syphilis in the pregnant woman. They stress the necessity for a searching examination of the past medical history of the families of both wife and husband, and while they perform a routine serologic test in their dispensary practice they show the difficulty of this procedure in private practice. The various signs and symptoms of syphilis in the history, in the pregnant woman, and in the products of conception of the syphilitic are fully described. It is interesting to note that they regard twin pregnancy, either uniovular or unichorionic, as a doubtful manifestation of syphilitic infection. The anatomico-pathologic features of the syphilitic infant are not given, but there is an excellent clinical discussion of the murderous effect of syphilis upon the ovum.

The question of the transmission of syphilis to the third generation is brought up in an excellent chapter on hereditary syphilis. The treatment of syphilis in its various clinical stages and in the various stages of pregnancy is outlined. The arsenicals, the mercurials and the bismuth preparations are discussed in detail.

A book of this nature will do much in the fight on congenital syphilis and well merits being read by anyone doing prenatal work. —Philip F. Williams

In the last decade or so, the general trend in medical and allied research has been away from mere reporting of slight morphologic and functional differences toward carefully planned studies of fundamental principles. Even fields like obstetrics and gynecology are applying more and more effort to the chemical and physical bases of normal and abnormal conditions. In fact this tendency is so widespread that frequently the title and subject matter of a paper may fail to reveal whether the work was done by a physiologist, chemist, surgeon, pathologist, internist, or obstetrician. This catholicism of research is a healthful sign. It is a hopeful promise of a fruitful future, especially if such books as the scholarly work of Dr. Needham on *Chemical Embryology*<sup>23a</sup> is a part of the movement.

A review of the available information upon the subject of Chemical Embryology has long been needed, but the stupendousness of the task has been a powerful deterrent to its undertaking. This need has now been admirably filled, in fact so well filled, that the three volumes are not only a storehouse of data, but also a powerhouse of stimuli for further work either in fields practically untouched, or in the clarification of specific subjects. The resulting experimentation should repay Dr. Needham in a measure for his years of labor.

Perhaps the best way to acquaint the reader with the scope of book is to enumerate the section headings: Embryology in Antiquity; Embryology from Galen to the Renaissance; Embryology in the Seventeenth and Eighteenth Centuries; The Unfertilized Egg as a Physico-Chemical System; On Increase in Size and Weight; On Increase in Complexity and Organization; The Respiration and Heat-Production of the Embryo; Biophysical Phenomena in Ontogenesis; General Metabolism of the Embryo; The Energetics and Energy-Sources of Embryonic Development; Carbohydrate Metabolism; Protein Metabolism; The Metabolism of Nucleins and Nitrogenous Extractives; Fat Metabolism; The Metabolism of Lipoids, Sterols, Cycloses, Phosphorus and Sulphur; Inorganic Metabolism; Enzymes in Ontogenesis, Hormones in Ontogenesis, Vitamins in Ontogenesis; Pigments in Ontogenesis; Resistance and Susceptibility in Embryonic Life; Serology and Immunology in Embryonic Life; Biochemistry of the Placenta; Biochemistry of the Placental Barrier; Biochemistry of the Amniotic and Allantoic Liquids; Blood and Tissue Chemistry of the Embryo; Hatching and Birth.

<sup>22</sup>Dépistage de la syphilis, en pratique obstétricale et prophylaxie de la syphilis héréditaire. By P. Rudaux et Montlaur. Préface du Docteur Cavillon. Masson et Cie, Paris, 1931.

<sup>23a</sup>Chemical Embryology (3 volumes). Joseph Needham, The Macmillan Company, New York.

The material is carefully, critically, almost fondly analyzed and sorted. Dr. Needham's extensive experimental work has ably fitted him for the task of evaluating the methods, the controls, and the results of the work that has been reported in the literature. Occasionally he accepts the result of a method that is still inaccurate, but there the method happens to be the best one used at present.

Numerous illustrations and tables are found throughout the volumes. The tables are an unusually valuable feature, as most of them contain in an itemized form practically everything known on the subjects, together with name of author and the year the work was done. The excellent features of this work are too numerous to even list. Experts in specific branches of chemistry who were asked to criticize sections of the books have offered nothing but praise.

Style in writing in general is not especially noted in a book where chemistry is the subject matter, but it is impossible not to mention the clearness, smoothness, and readableness of the text, done in the best English tradition of scientific writing. In this connection the reviewer cannot help but call attention to the fascinating chapters devoted to the philosophy and the history of chemical embryology.

One can go on and on, but the sum and substance of the remarks would merely be that Dr. Needham has written an unusually excellent and valuable book that cannot be recommended too highly to the obstetrician who wants to know his work from its very beginning and not only at its ending.

—S. H. Gray.

#### MISCELLANEOUS

This is a very valuable little book<sup>30</sup> which every physician should read and possess as it contains a fund of important information. The author is correct in stating that "The principles governing the relationship of patient and physician must be sensed and felt, rather than defined. The law has laid down only the more obvious rules. The doctor with fineness of mental perception will discern for himself the subtle character of the relationship, and the quality of its obligations. If his intuitive sense of what is true, right and proper does not lead him to avoid the more obvious pitfalls, no book can help him. Nevertheless, he should know the elementary things which the courts have said upon this subject." Many important questions are taken up in detail. For example, "His implied engagement with his patient does not guarantee a good result, but he promises by implication to use the skill and learning of the average physician, to exercise reasonable care and to exert his best judgment in the effort to bring about a good result." Physicians should also remember that "A physician who holds himself out as being specially versed in some phase of medicine is required to possess special knowledge and skill, not merely such knowledge and skill as the *average physician* has, but such as is possessed by the *average specialist*." "All the obligation is not upon the physician, but the patient also has his duties to discharge. In particular, the patient must obey the orders and follow the directions of his physician . . . ."

Valuable information on confidential communications will be found, including the ruling that payment of a fee is not essential to the relationship of physician and patient. The question of when confidential communications may be waived in court is likewise discussed.

The important question of malpractice is very fully dealt with, including such important subjects as breaking of hypodermic needles, leaving behind of gauze packs, x-ray burns, etc., as well as the physician's responsibility for the actions of interns, nurses, etc. Defense to actions for malpractice, expert testimony, the doctor on the witness stand, and the doctor in criminal law, are the main topics discussed.

This book is well written, short and concise, by a man who for many years was the general counsel for the Medical Society of the State of New York.

—R. T. Frank

<sup>30</sup>**Courts and Doctors.** By L. P. Stryker. The Macmillan Co., New York, 1932.

Barger who has contributed so much to our knowledge of the chemistry and pharmacology of ergot has elaborated the Dohme Lectures into an excellent monograph.<sup>31</sup>

After a historical review of the knowledge of ergot and its poisonous effects, the symptoms of ergotism and its geographical distribution are outlined. The author calls attention to the problem presented by the two clinical types of ergotism; namely, the convulsive and the gangrenous. Based mainly on E. Mellanby's observations, he suggests that a vitamine A deficiency may be an essential feature in producing the convulsive form of ergotism. The botanical, chemical, pharmacological and clinical aspects of ergot are completely covered. A discussion of the problems involved in a proper standardization closes the volume to which an excellent, complete bibliography is appended.

Barger has provided us with a standard work which will serve as a welcome starting point for all future studies in extending our knowledge of ergot and its actions.

—S. Silver

Graves' *Female Sex Hormonology*,<sup>32</sup> a review according to the preface, is designed primarily for the student who has little previous knowledge of the subject and therefore no attempt at a critical survey is to be expected by the reader. The individual chapters include the sexual cycle in animals as well as in the human being, and attempt a correlation of the various cycles together with a discussion of the paramount rôle of the hypophysis in sex physiology.

Unfortunately the author has not fully succeeded in his endeavor, perhaps partly because the entire subject is as yet in a state of flux. It appears to have been hurriedly written and contains many errors. For example, the average physiologist would take exception to the definition of "the word oestrus as it is most commonly used at the present time relates to the specific genital changes that can be induced in laboratory animals by the injection of certain ovarian and hypophysial substances." Again "if impregnation does not take place the sexual cycle ends with the death of the ovum, . . . ." Dates of publication, crediting discoveries to authors who have had no participation in the work, etc., abound. For example, the isolation of the female sex hormone in crystalline form was published by Doisy alone, not by Allen and Doisy as mentioned on page 39.

The author has shown a great fondness for inventing new names, as for example "dysfunctional" instead of "functional," "dysplasia" instead of "hyperplasia," for which no good reason appears to exist.

—R. T. Frank

In his preface, Livingston states that his *Clinical Study of the Abdominal Cavity and Peritoneum*<sup>33</sup> was written with particular reference to the abdominal signs and symptoms as well as their causation. The book was designed for the student and the clinician as a reference book. For the most part it is a compilation rather than an original composition.

This is a large volume gotten up in elegant form, with numerous illustrations, the great majority being from other sources to whom due credit has been given, and reference further aided by marginal headings.

The sections of the book contain the following—the peritoneum regarded as an empty cavity; the gastrointestinal tract; visceral neurology; innervation of the gastrointestinal tract as a whole. The other chapters dealing with the sympathetic division of the involuntary nervous system, the parasympathetic system, the vis-

<sup>31</sup>*Ergot and Ergotism*. By George Barger, F.R.S. Gurney and Jackson, London, 1931.

<sup>32</sup>*Female Sex Hormonology*. A Review. William P. Graves. W. B. Saunders Co., Philadelphia, 1931.

<sup>33</sup>*A Clinical Study of the Abdominal Cavity and Peritoneum*. Hoeber's Surgical Monographs. E. M. Livingston. Paul B. Hoeber, Inc., New York, 1932.



cerogenic reflexes, and the gastrointestinal reflexes, will prove of real interest because in them are gathered facts which ordinarily can be found only scattered in the literature, and because of the excellent demonstration charts contained therein. The final chapter deals with clinical interpretation of viscerosensory phenomena (skin signs).

For the reader who desires to find information rapidly, particularly information with reference to the basic literature, this book should be of great assistance. The embryology, physiology, and the principles of all the abdominal intestinal operations are taken up in short but informative fashion.

The last 100 pages of the book are somewhat in the nature of padding even though they might prove of real interest to the reader, including the commoner eponyms associated with names of well-known medical men, with reproductions of the basic articles describing them. For example, Sir Christopher Addison, Courvoisier, Henry Head, McBurney, etc., as well as a questionnaire designed for students. Reference to the literature would have been greatly simplified if arranged according to the alphabet.

—R. T. Frank

This volume deals with the subject of roentgen therapy<sup>34</sup> in benign and malignant conditions other than those that are usually included in dermatology.

It is divided into four parts; the first part deals with the theoretical physical background of x-rays; the second part considers the biologic response of the various tissues of the body to radiation; the third part describes the different methods of application; and the fourth part discusses the clinical application of roentgen therapy.

In general the book covers adequately the field usually known as deep x-ray therapy. In the third part under the general methods of irradiation, the works of Wintz and Warnekros are compared and fully discussed. It is surprising that a volume written by a Frenchman should omit the Coutard method which is being so widely used at present.

Under treatment of carcinoma of the cervix the author describes Wintz's method of ionization with copper and selenium for the sterilization of the secondary infection of the neoplasm and for the production of increased secondary radiation. He also strongly advocates its use. This procedure is no longer used in the large cancer clinics and its efficacy is questionable.

Mention is made of combining Curietherapie (radium) with x-ray therapy in carcinoma of the cervix. There is, however, very little discussion of radium, either concerning its properties or clinical application in the treatment of neoplasms.

The chapters on the treatment of benign conditions such as Basedow's disease, uterine fibroids, local infections, adenoma's of the pituitary, etc., are brief but adequate for a guide where radiotherapy may be used with benefit.

The author gives his reasons for objecting to the use of radiotherapy in the induction of therapeutic abortion. They are based entirely upon theoretical grounds and undoubtedly have not taken into consideration the favorable clinical reports made in America and Switzerland on the subject.

The volume may be recommended for the student and practitioner in radiotherapy as a concise work in the main expressing the views of the leading men in radiotherapy as to physics and radiophysiology. The clinical aspects necessarily must be sketchy in a book of this size; for a complete understanding recourse to original sources is essential. There is a bibliography covering the authors mentioned in the book.

—William Harris

<sup>34</sup>**Radiotherapie (Technique du dosage en profondeur).** Ch. Guilbert avec la collaboration du Dr. Jean Quivy pour la partie physique. Editions Medicales N. Maloine; Paris, 1932, pp. 437.

# Department of Reviews and Abstracts

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CONDUCTED BY HUGO EHRENFEST, M.D., ASSOCIATE EDITOR

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## Selected Abstracts

### Abortion

Leunbach, H. J.: A New Form of Intrauterine Therapy Consisting of the Injection of an Antiseptic Paste Into the Uterine Cavity. *Monatschr. f. Geburtsh. u. Gynäk.* 87: 509, 1931.

The author recommends the use of an antiseptic paste chiefly for the purpose of bringing about therapeutic abortions. It is therefore essentially a substitute for curettement. The injection of this paste can be performed by any physician and it does not require hospitalization of the patient. The author has used this procedure for the last three years and is enthusiastic about it. Uterine contractions do not begin until about 12 hours after the instillation of the paste and in about twenty to thirty-six hours the contents of the uterus are expelled. If the pregnancy is less than five weeks old the whole ovum is usually expelled intact. If the pregnancy is six to twenty-one weeks old, the fetus is usually discharged in twenty to thirty-six hours and the placenta follows a few hours later. The paste is absorbed within forty-eight hours. In most cases there is no febrile reaction at all and in only 4 out of the author's 100 cases was a curettement necessary after the use of the paste. If the substance is used in a pregnancy of more than twelve weeks' duration, the expulsion of the uterine contents is similar to that in full term labor.

The uterus is not harmed by this procedure and in one instance a new pregnancy was started two months after the use of the paste.

J. P. GREENHILL.

Wolf, H.: Induction of Abortion by Means of Intrauterine Application of a Paste. *Monatschr. f. Geburtsh. u. Gynäk.* 88: 442, 1931.

In 12 cases Wolf induced therapeutic abortion by introducing a paste into the uterine cavity which contained iodine, thymol, camphor, eucalyptus, myrrh and other ingredients. Following instillation of the paste, the patients rested for four hours and then were permitted to leave for their homes. After ten to twelve hours uterine contractions usually set in and this was accompanied by bleeding, but in no case was there a real hemorrhage. On the contrary the amount of blood lost in these cases was less than usual in cases of abortion. The fetus and placenta were expelled on an average of twenty hours after the introduction of the paste. The author believes his good results warrant the further use of this method of inducing abortion. In the hands of trained individuals there is no danger at all. One special advantage of the method is that patients need not remain in bed. In fact, bodily activity helps to expel the ovum.

J. P. GREENHILL.

Wagner, G. A.: The Question of Interruptin. *Monatschr. f. Geburtsh. u. Gynäk.* 90: 445, 1932.

Wagner discusses the use of pastes for the purpose of producing abortions and emphasizes that in one-quarter of the cases the ovum was actually expelled without complications. In some cases the pains were unusually severe, and in others the ex-

pulsion of the ovum was prolonged for five or six days and had to be completed by digital or instrumental manipulation. In some instances there were severe hemorrhages. These facts coupled with the fatalities which have followed the use of these pastes, stimulate Wagner to warn his pupils against the use of these pastes. The latter are particularly dangerous when they are used in a case where an abortion is in progress. In such cases it is very easy for the paste to be injected into the maternal blood stream and lead to a paste embolism. J. P. GREENHILL.

**Sellheim, H.: Interruption of Pregnancy by Means of Injection of Pastes. Their Dangers and Attempts to Disclose These Dangers.** *Monatschr. f. Geburtsh. u. Gynäk.* 90: 441, 1932.

Sellheim employed intrauterine injection of pastes to interrupt pregnancy in about 80 cases. He experienced one death after its use but autopsy failed to reveal the cause of death. Whereas Sellheim's experience was favorable, others began to report serious complications of fatalities. Thus according to Engelmann there have been 22 deaths from the injection of these pastes into pregnant uteri. Deaths are due to four causes, (1) air embolism, (2) fat embolism, (3) perforation of the uterus and entrance of the pastes into the peritoneal cavity with shock, and (4) unknown causes. Sellheim believes that air emboli, fat emboli and uterine perforation can all be avoided. For the class of unknown deaths he believes the responsible factor is poisoning due to escape of the paste into the maternal blood stream. He proved this experimentally in animals. J. P. GREENHILL.

**Leunbach, J. H.: Concerning the Paste Method of Producing Abortion.** *Monatschr. f. Geburtsh. u. Gynäk.* 90: 446, 1932.

Leunbach is of the opinion that the dangers of paste injections can be eliminated by observing the following rules: (1) Only those pastes should be used which are guaranteed by the manufacturers to be absolutely free of air. This may be controlled by means of inspection. Further the pastes should be soluble in water to avoid the danger of fat embolism and they should not contain free alkali or other poisonous substances. (2) An attempt should be made to be certain there is no serious infection in the vagina or the cervical canal. The antiseptic properties of the pastes do not guarantee against sepsis. (3) In cases of cardiac decompensation an effort should be made to restore compensation. (4) The pastes should not be used during the first six weeks of pregnancy. (5) From the sixth to the twelfth week, the pastes are excellent for the induction of abortion but one should be ready to follow this with a curettement. (6) Between the third and fifth months of pregnancy pastes are the best and easiest means of inducing abortion. (7) Pastes appear to be well adapted for the induction of labor. J. P. GREENHILL.

**Strassmann, G.: Death From Air Embolism After Criminal Abortion.** *Monatschr. f. Geburtsh. u. Gynäk.* 81: 269, 1929.

In a series of 60 deaths which followed criminal abortions and which were autopsied by the author he could find only five definite cases of air embolism and one additional case where it was difficult to make a diagnosis between protracted air embolism and acute, fulminating sepsis. Most of the deaths which heretofore were attributed to shock are now known to be due to air embolism. It is generally difficult to prove the presence of an air embolism because the bodies are examined too late after death, thus permitting the formation of decomposition gases. In the author's clinic, O. Schmidt has perfected a test whereby the difference between these gases and oxygen can be detected. The author reports in detail his six cases and maintains that in all cases of rapid death in women during the child-bearing pe-

riod, we must think of air embolism. In some instances, the air-containing fluid used to produce the abortion may remain in the uterus and only after separation of the ovum from the uterine wall will it be sucked into the circulation and produce death.

J. P. GREENHILL.

**Peller, S.: Abortion and Decrease in Births.** *Med. Klin.* 27: 847, 1931.

At the present time, according to Peller, there are probably one million or more abortions annually in Germany. In Vienna the frequency of repeated abortions has increased since the war. This is also true in Moscow and Leningrad. It has been found that abortions are more common in cities than in the country. In large cities approximately 50 per cent of all pregnancies end in abortion but this does not mean that all the abortions are induced. In large cities, a high proportion of the births are regulated by preventative measures but this is not as true in the country. The older the women the more they tend to restrict conception in the cities but this is not true in the country. On the other hand, abortions after forty years of age are much less common in cities than in the country.

In the small cities births are controlled more by abortion than by preventatives whereas the reverse obtains for the large cities.

Illiterate women more frequently resort to abortions than literate ones. Likewise the Jewesses of Russia seldom have abortions performed. The legalization of abortions in Russia has led to a reduction in mortality and frequency of complications usually associated with these operations.

J. P. GREENHILL.

**Harbitz, H. F.: Etiological and Clinical Investigation of Abortions Treated in the Oslo Municipal Hospital Between 1920-1929.** *Acta obst. et gynec. Scandinav.* 11: 50, 1931.

Of 3791 cases of abortion treated in the Oslo Municipal Hospital more than half were febrile. The majority were most likely criminal in origin. The total death rate was 2.16 per cent. Among the 129 women who had complications on admission to the hospital the mortality was 34.1 per cent whereas among the 3,662 without complications it was only 1 per cent. In the febrile cases the death rate was ten times as high as among the afebrile cases.

The treatment of the uncomplicated cases was both expectant and active. Of the febrile cases, 60 per cent were treated actively, 29 per cent expectantly and 11 per cent conservatively. The mortality was a trifle lower in those not treated actively. The most frequent cause of death was purulent peritonitis. Clinical thrombosis and embolism occurred in 0.77 per cent of the cases.

J. P. GREENHILL.

**Bronnikowa: Labor After Artificial Abortion.** *Zentralbl. f. Gynäk.* 53: 292, 1929.

From the State University of Moscow 1470 cases of labor occurring after previous abortions are analyzed with the following results: In general, pathologic labors occurred more than two times as frequently as in control cases without previous abortion (13.8 per cent and 6.8 per cent respectively). During labor, and immediately following, atonic bleeding was nearly 2 times as frequent, adherent placenta 3 times, weak labor pains 4 times, Credé expression of placenta, manual removal, etc., nearly 3 times, and forceps were used 8 times as frequently as in a similar series of cases which had not undergone previous abortion. Puerperal complications (endometritis and lochiometra prevailing) were nearly 2 times as frequent. The average size of the baby was slightly but definitely lower in those cases with previous abortions, but the placental weight was definitely greater, seeming to show, as the author expresses it, "an expression of the struggle for existence of the fetus."

WILLIAM F. MENGERT.

Levit: Induced Legal Abortion and Its Sequelae. *Zentralbl. f. Gynäk.* 53: 808, 1929.

A series of 2930 induced, legal abortions, done by curettage between the years of 1913 and 1926 are reported from the State University clinics of Gynecology and Obstetrics at Leningrad. The following observations on the sequelae of these abortions are given: Mild infections postcurettage, as evidenced by slight temperature reactions, are often the cause of subsequent difficulties, such as extrauterine pregnancies and sterility. In 204 cases of extrauterine pregnancies in the clinic during these years, 85 cases had had previous induced abortions. Since induced abortions have been done, the yearly percentage of extrauterine pregnancies has risen from 1.5 per cent in 1917 to 5 per cent in 1926. Curettage to terminate pregnancies has been the cause of chronic, ambulatory infections, and affections of the genital organs in 20 per cent of the cases. Some of these sequelae are: secondary sterility, residual peri- and parametritis, perisalpingitis, endometritis, metritis, and extrauterine pregnancy. Perforation of the uterus was rare, as there were only 3 cases in the series.

WILLIAM F. MENGERT.

Bué, V.: The Artificial Interruption of Pregnancy. *L'Écho Médical du Nord.* 23: 269, 1929.

From the judicial standpoint, responsibility in the induction of abortion depends on the will and intention of the agent. For the physician, the following conditions must be satisfied: (1) That the mother is in extreme danger; (2) That this danger is entirely due to the pregnancy; (3) That therapeutic abortion will surely alleviate the danger, and (4) That other therapeutic measures have completely failed.

The application of these conditions is entirely a matter of the physician's conscience. Such diseases as hydatiform mole, severe hemorrhages, hydramnics, the cardiopathies, and renal affections call for intervention.

In handling the tuberculous case 3 factions exist: Those who almost always terminate pregnancy, essentially physicians outside of France; those who intervene in exceptional cases, French physicians; and those who never intervene, the majority of French physicians. In defense of the French viewpoint there is: (1) The progeny if removed from the home need not develop tuberculosis, especially since treatment with B. C. G. has proved so efficacious. (2) The belief that pregnancy always causes an aggravation of the tuberculosis is not supported by the clinical facts. Moreover, the danger appears in the last three months when everybody agrees that intervention should not be instituted. With this in mind, if abortion is induced during the first three months, the law is broken since there is no extreme danger during this period. (3) Whether or not the pregnancy is a grave menace is difficult to ascertain, as the tuberculosis is present and in itself a grave menace. (4) The traumatism associated with induction of abortion may aggravate the tuberculosis. (5) There is no clinical method which will aid in recognizing in advance the case in which interruption of pregnancy will be favorable or injurious. The sole certainty is that an infant has been sacrificed.

In cases of pregnancy with tuberculosis, it is best that the tuberculosis be taken care of and the gravidity let alone. Intervention should be practiced only during the first three months and only with the firm conviction that if nothing is done both mother and child will be lost due to a lighting up of the process.

In the consideration of pernicious vomiting of pregnancy, the author believes that there are cases in which intervention is necessary, but these are rare.

As far as eugenic indications for the interruption of pregnancy are concerned, the following factors must be considered: (1) Do we know enough about the laws of heredity? (2) Can we not by means of education counterbalance possible defects

due to heredity? (3) Has the time come when childbirth is to be further restricted (in France)?

Interruption of pregnancy for eugenic reasons is not defensible.

FRANK SPIELMAN.

**Wohlwill and Bock: Infections of the Placenta and Fetal Sepsis.** Arch. f. Gynäk. 135: 271, 1929.

The authors describe in detail four cases of true placentitis in each of which pregnancy was of four or five months' duration. *B. coli* were found in two cases, streptococci in the third and *B. coli* and a gram positive anaerobe in the fourth. Each of the four cases definitely followed a fetal sepsis which resulted in metastatic placental infections. The chorionic villi always showed the greatest amount of infection. The first patient died from a *B. coli* sepsis following first a fetal sepsis and secondly a placentitis. In two of the cases there was no resulting maternal infection following the fetal sepsis and placentitis. The fetal tissues with the exception of the placentae and possibly the fetal livers showed no reaction to these infections when examined microscopically, apparently the four or five months' old fetus cannot respond to infections by the formation and outpouring of leucocytes.

RALPH A. REIS.

**Vogt-Möller: Treatment of Habitual Abortion With Wheat-Germ Oil (Vitamin E).** Lancet 221: 182, 1931.

Vitamin E is found in certain vegetable oils, especially in wheat-germ, maize, and lettuce, while little or none is found in animal oils. A deficiency of this vitamin causes in the female a seeming sterility due to early resorption of the implanted ovum.

The author reports two human pregnancies carried to viability, probably because of the administration of wheat-germ oil in 5 c.c. amounts daily in early pregnancy for a fortnight, after which it was decreased gradually to 5 c.c. every sixth day.

Even on an ordinary diet it is possible that some individuals may suffer from hypovitaminosis E.

H. CLOSE HESSELTINE.

## AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY

Members of this Board, as well as those of the other specialties, and many of their Diplomates are constantly being asked about the purposes of these Boards, the value of the certificate, its advantages to the Diplomates, and other matters of general interest. It is planned to publish from time to time through the courtesy of the Editor of the AMERICAN JOURNAL OF OBSTETRICS AND GYNECOLOGY short notes answering these and other questions for the American Board of Obstetrics and Gynecology (see July and August issues).

### VALUE OF CERTIFICATE

The certificate is of value to the Diplomate in many ways, and it is confidently expected that both the medical and the lay public, including hospital directors and other authorities, will soon consider it an official and authoritative means of discriminating between those qualified as specialists in obstetrics and gynecology, and the self-styled specialist.

Certain hospitals are considering the requirement of a certificate for Staff appointments, and the national obstetrical and gynecological organizations participat-

ing in the formation of the Board, as well as other societies, attach considerable importance to its certificate. The American College of Surgeons accepts the certificate in lieu of certain of its requirements in obtaining Fellowship.

The names of all new Diplomates are regularly announced in the AMERICAN JOURNAL OF OBSTETRICS AND GYNECOLOGY; lists of those holding certificates who are limiting their practice to obstetrics and (or) gynecology are issued from time to time by the Board, and will also appear in the Directory of the American Medical Association. This latter also indicates by a numerical symbol in the biographic data of those whose names are eligible to appear on these lists, that they are Diplomates of this Board.

It is only reasonable to expect that in the reference of patients, for example, in instances where the Directory of the American Medical Association is used that preference will be given, not to a man who has merely the self-assigned OBG. after his name, but to one who has the official approval of the Board as shown by the numerical indication of his certification (now 10). The Board's own directory is in the office of each active Diplomate.

The three national organizations which elect the Board members and the Board, are determined to maintain high standards for certification in this group although any well qualified obstetrician and gynecologist should have no difficulty in obtaining the certificate. It is intended also, as time goes on, to use every possible means of impressing the medical and lay public with the official importance of this certificate.

It has been proposed that a luncheon and Round Table Conference be held at the time of the annual meeting of the Board on the first day of the American Medical Association convention. At this time new Diplomates would be introduced in person to those present for the convention, old acquaintances would be renewed, and new friends made. A general discussion of Board aims and activities would follow. Plans for this, if approved, will be announced later.

It should be considered an obligation upon every older and well-established obstetrician and gynecologist to obtain the certificate because of the example he sets for the younger men. Its value to him is less personal than it is that the Board needs his active participation in the advancement of obstetrics and gynecology in the United States and Canada.

The advantages to the younger men have been outlined. It is to be hoped that by them the holding of this Certificate will soon come to be looked upon as a necessity.

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#### NEXT EXAMINATION

The next written examination and review of case records is to be held on Saturday, October 22, 1932, at 2 P.M. in nineteen or more cities of the United States and Canada. Application should be made immediately. Necessary application forms and detailed information may be obtained from Dr. Paul Titus, Secretary, 1015 Highland Building, Pittsburgh, Pa.

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## American Gynecological Society

Fifty-Seventh Annual Meeting

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### THE CONSTITUTIONAL FACTOR IN GYNECOLOGY AND OBSTETRICS\*

GEORGE GELLHORN, M.D., F.A.C.S., ST. LOUIS, MO.

IT SEEMS that almost every newly elected President has felt the urge to go back to first principles, to look through our old Transactions, and to become familiar with all the work this Society has done in the past. At any rate, that was exactly what I did, and I learned a great deal from this study and experienced a new respect for old achievements.

At the same time I was greatly interested to see how far Gynecology had traveled since that day in 1876 when our leaders first assembled in New York. At that time, and for almost thirty years after, Gynecology concerned itself exclusively with the pathology of the various organs of reproduction and concentrated practically all its efforts on perfecting the surgical treatment of the diseases of these organs. As Aschner puts it, the gynecologist was merely a uterologist.† The cause of disease was still a matter of speculation, and there was no unanimity of opinion except that it was due to some *external* force. The discovery of microorganisms offered the first hope of the solution of this problem. "Bacteriology came like a beam of light into the darkness" (Brown). The phenomena of disease were now readily interpreted as the effect of bacteria upon the cells of the body, and, to quote Brown once more, if any deviation from the normal or expected course of events occurred, it was attributed to some change affecting the microorganism. That man is not merely a culture medium, that the host, too, plays an important part in the interaction between the body and the infecting organism, was recognized only at a later stage.

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\*Presidential Address, Read at the Fifty-Seventh Annual Meeting of the American Gynecological Society, May 30 to June 1, 1932, at Quebec, Canada.

†Etymologically, hysterologist would be a more correct expression.

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NOTE: The Editor accepts no responsibility for the views and statements of authors as published in their "Original Communications."



Meanwhile the first timid beginnings of endocrinology established the truth that in some cases the cause of disease may reside *within* the body, and so our eyes were drawn from the diseased organ to the diseased organism, from the cell to the patient as a whole. We were then impressed by the fact that patients differed from each other in many respects. This was by no means a new discovery. A hundred or more years ago our medical forefathers spoke of "temperaments" as distinguishing criteria, and these denominations were replaced, in the first half of the nineteenth century, by such terms as diastheses and dyscrasias, until, in 1858, Virchow's Cellular Pathology drove all these remnants of the humoral pathology of Hippocrates, Aristotle and his followers into the limbo.

Now, however, the observations made on the endocrine glands, investigations into the nature of the vegetative nervous system and studies of metabolism deflected medical thought away from a purely morphologic conception towards a biologic point of view, and today the study of constitution approaches the problem of individual differences from a wider and more scientific angle. An amazingly large amount of work has already been done in a very short time, particularly in the field of internal medicine where Martius, Krauss, Brugsch, Bauer and others led the way. In the steadily mounting literature with specific reference to gynecology and obstetrics, the monographs by Sellheim, Aschner, Mathes and especially the encyclopedic treatise by A. Mayer demand attention. In America, our fellow member, Charles P. Noble was the first, and as far as I know, the only one to write specifically on the constitutional factor in our specialty.

But this branch of science is still so young and the problem so intricate and controversial that we are only at the threshold of a new and enticing territory. The very definition of the word "constitution" presents difficulties because this term, though in daily use, does not connote the same meaning to everybody. Primarily, Constitution implies something inherited, something that was established when the chromosomes of the parental gonads first united. The combination of hereditary traits which determine the outer form, the physiologic functions, and the mental processes of an individual, forms the basis of his constitution and represents his "genotype."

According to some writers, notably Tandler and Bauer, the genotype remains essentially unchangeable though slight variations may occur later.

Opposed to this conception of the immutability of constitution is the view held by the majority of observers, that external forces have the power of producing more or less pronounced alterations and modifications of the genotype. These accessory influences may make themselves felt in utero, but for the most part, they operate in postnatal life. They comprise prematurity, birth injuries, unsuited artificial feeding, the so-

called children's diseases and other severe infections, climate, unhygienic living conditions, lack of air and light, malnutrition, etc., and their influence may, in point of time, extend until about the appearance of puberty. The product of heredity, then, plus the influence of environment combine to give to the person his true individuality, his constitution. This wider concept of constitution is termed the phenotype of a given individual.

The phenotype need not be evident at once; it may not put in appearance until puberty or even the climacterium when the dominant features of the constitution come into preeminence. Even the superficial lay observer then notes that this or that person has "changed completely."

Let us further remember that the inherited potentialities of constitution react in a particular way to stimuli of any kind and, thus may create in one person a marked resistance, in another an undue susceptibility to disease. In short, "constitution is the morphological, physiological and psychological resultant of the properties of all the cellular and humoral elements of the body; this resultant is determined by the laws of heredity and by the influences of environment" (Pende).

#### CONSTITUTIONAL TYPES

Whether we adopt this or any other definition, we must admit that the constitution is unique for any given individual, that no two persons can have exactly the same constitution.

There are, however, enough similarities to permit us to classify all human beings into various groups or types. The literature contains many such classifications based on the assumption of two, three or more fundamental types with numerous subdivisions, combinations and blendings. The simplest groupings are, perhaps, anthropometric divisions into the long-thins and short-thicks (Draper) or the slender, medium, and stocky (Bell). The French School (Sigaud, Chaillou, Mac Auliffe) laid emphasis on function and distinguished four types: *type respiratoire, digestif, musculaire* and *cerébral*. Krauss, Martius, Krehl and others saw in constitution the sum total of resistance and counteraction to environment; and to yet another group of workers the accentuation of mental processes appeared essential in the classification of individuals (Kretschmer).

As most authors have found it desirable to coin designations of their own in order to stress the most distinguishing trait, there has sprung up a highly complicated nomenclature which renders the study of constitution somewhat confusing. In our special field of inquiry, however, we may avoid this multitude of terms which are based largely upon observations on *men*, and attempt to study the differences existing between *women* by adopting Tandler's classification into hypotonics, hypertonics and, between them, those of normal tonus. It may well be that at some future time physicochemical determinations (Saltykow) or other

highly refined methods of examination (Mathes) will simplify matters. For the present we must perforce be satisfied with less exact definitions. This at once applies to the term, "normal tonus." Nobody can tell accurately just what is a "normal" woman. We can only have a sort of intuitive conception. Rafael's Sistine Madonna impresses us as normal, and so does, in the plastic art, the Venus of Medici. The "normal" woman is of moderate height; her lower limbs are short in proportion to the trunk, and the thighs are in close apposition; the bones are delicate, the wrists and ankles slender, the breasts round and firm; the pelvis is broad, the arch of the foot not very high; there is no hair on the body except on the pubes and, less copiously, in the axilla; the face is small, the neck small and round; the costal angle is wider than 90 degrees; the outer contour exhibits soft curves, and the buttocks are firm and prominent; the skin is thin, tight, and elastic. These are only some of the physical characteristics of the normal woman, but such perfect types are rare. Together with such a physique, the normal woman functions, reacts to environment, and responds to mental and psychic stimuli in a way which, again prompted more by artistic feeling than by exact measurement, we call harmonious. Other things being equal, such a woman will menstruate normally; she will conceive readily, pass easily through pregnancies and labors, and have abundant milk supply in the puerperium. The chief endowments of this ideal in total human development, according to W. W. Graves, seem to be symmetry, proportion, harmony, and adaptation of structures and functions. As physicians we seldom come in contact with these types in a professional way because their very attributes seem "to supply them with those peculiar qualities which enable them to adapt themselves well to their environment, to resist disease, to survive and to attain long life."

The other two types are the ones which we find most frequently in our patients.

The hypotonic type includes asthenia and infantilism as well as the "intersexual type" of Mathes.

Among the first to describe the asthenic woman was our fellow member, Richard R. Smith. Although his paper, presented before this Society in 1906, dealt specifically with enteroptosis, he did not fail to notice certain general characteristics which went hand in hand with the downward displacement of the abdominal viscera. He observed that these women exhibited (1) a flabbiness or hypotonus of the body tissues; (2) a lack of vital energy; (3) a more or less pronounced backwardness in development. "If we examine such patients," he continued, "we note a long, narrow, shallow, and usually more or less collapsed thorax, flaccid abdominal walls, usually a prominent abdomen, changes in the curves of the spine, a general relaxation and flabbiness of the muscular and connective tissue structures, and, as a rule, an abnormal lightness in weight. There is a ptosis of the abdominal viscera and, perhaps, a

displacement of the pelvic organs. Combined with these objective symptoms we find a list of subjective phenomena the principal ones of which are: general weakness, an inability to carry on work without exhaustion, nervousness, oftentimes melancholy, constipation, and disturbances of digestion and other functions, such as those of menstruation and urination. Such patients commonly have backache, pain in the lower abdomen in one or both sides, a bearing down sensation, leucorrhea."

One year after this paper by Smith there appeared the classical treatise by Stiller which affixed the term *Asthenia* to this type of human beings. Parenthetically, *asthenia* is not a new word. It has been in use for more than a hundred years and has always been employed to denote a sickly, feeble, pathologic condition. Viewed from the angle of constitution, *asthenia*, however, does not necessarily mean sickness. Many *asthenics* may be healthy all their lives (Hofstaetter) and even live longer than so-called stronger people (Saltykow). In the female, *asthenia* does not often manifest itself before puberty, and it usually ceases after the menopause coincidentally with the accumulation of fat. It is, however, undeniable that during the reproductive age the demands of life are too great for the large majority of *asthenics*. In all likelihood it is something connected with the sexual life which disturbs their equilibrium (Hofstaetter); but there may be stress of some other kind under which their latent weakness often appears (Wood). Such women form the greater part of our gynecological patients.

The best known example of the *asthenic* woman is the *Venus of Boticelli*. She corresponds closely to the description given to us by Smith. While the stature of *asthenic* women is usually below the normal, a considerable percentage must be classed as tall. In any case, the lower extremities are disproportionately long. The face is long and narrow, the skin thin and transparent, the neck is long and the shoulders slope downward; the clavicles are prominent with marked supra- and infraclavicular depressions, the scapulae which in the "normal" woman lie flat on the thorax, project outward, the epigastric angle is acute, and the ribs slant steeply downward. The posture of the *asthenic* with its high dorsal kyphosis and low lumbar lordosis is quite characteristic. ("Gorilla" type posture of Dickinson.) Stiller considered the floating tenth rib as a definite and constant finding in *asthenia*, but this is no longer generally accepted. In this connection, attention should be given in gynecological circles to the scapular classification in relation to constitution to which W. W. Graves has devoted years of painstaking investigation. A relatively large number of *asthenics*, according to Graves, bear the type of scapula designated "scaphoid." Hernias and flat feet are also frequent findings.

The configuration of the thorax and the general laxity of muscular and connective tissue structures account for the pendulous abdomen and the ptosis of all viscera. The latter again gives rise to obstinate

constipation, and this in turn to disturbances of nutrition. Constipation is also a prolific source of gynecological ailments, for the long retention of feces in the ampulla recti may cause a thickening of the sacrouterine ligaments which may lead to posterior parametritis and, secondarily, to uterine displacements. The concomitant congestion of the pelvic vessels may cause an irritation of the pelvic peritoneum which, finally, would result in dysmenorrhea, menorrhagia, vaginal discharge, and pain in coition. That this syndrome might eventually lead to dyspareunia, frigidity, and vaginismus is not surprising, *for the somatic asthenia has its counterpart in psychasthenia and hyperesthesia*. Mayer who graphically describes this course of events, also points out how such patients are apt to fare when they consult a physician. There are two rather common eventualities. Complaining of some gynecologic symptom such as backache, the examiner on finding no gross abnormality may declare the patient healthy but imaginative, and this unsatisfying attitude may eventually drive the woman into the hands of a cultist or a quack. More frequently, however, a gynecological ailment is diagnosed and local or surgical therapy instituted instead of searching for the underlying constitutional cause which would call for treatment of constipation, inanition, or exhaustion. This is no mere speculation, but a matter of real practical importance. With rare unanimity all students of the question speak of the increasing frequency of asthenia even though Aschner's estimate of 70 per cent may be regarded as too high. Let us further remember the numerous instances where such patients, after the first suggestive effect of an operation has worn off, come back with the same complaints.

Infantilism represents a separate type in which the development of the body has been arrested as a juvenile stage. Consequently, the infantilistic individual exhibits physical and psychical traits reminiscent of the child. This expresses itself externally in the youthful appearance, the round chin, the proportions of the skeleton, the cylindrical thorax and the course of the ribs which run at right angles to the spine. The secondary sexual features are incompletely developed; the hard palate is narrow and high; the front teeth are widely spaced ("trema" and "diastema"). In the genital sphere the hypoplasia of the external organs is often very marked. The configuration of vagina and cervix presents a typical picture. The small uterine body lies in pronounced anteflexion, retroflexion or lateroflexion or exhibits other signs of arrested development (arcuate, rudimentary uterus, etc.). Both the external and internal os are small. The tubes are too long and tortuous;\* the ovaries are small and smooth from lack of ovulation. The culdesac is abnormally deep, and this, together with a primary weakness of the pelvic floor, may give rise to prolapse of uterus or rectum in children and nulliparous women; in such instances a spina bifida occulta is often

\*This has long been recognized to be one of the etiologic factors of tubal pregnancy.

found on x-ray examination. The small pelvis with its narrow arch, its funnel-shaped outlet, and its insufficient inclination completes the picture, not to mention the infantile appendix, the elongated bladder, the small heart, and the narrow aorta. The endocrine system is profoundly affected, particularly in the sense of hypofunction of the pituitary body and the ovaries.

Psychically the outlook on life, the instability of the nervous system, the unwilling response to sexual demands (frigidity, dyspareunia, vaginismus) are further evidences of stunted growth.

The hereditary cause of infantilism can in many cases be traced to alcoholism or syphilis of the parents or to pre- or postconceptional exposure of the mother to x-rays. In postnatal life anything that retards the development of the infant may become responsible for infantilism, be it directly through poisons or infectious diseases or by way of disturbing the endocrine balance.

Infantilistic girls begin to menstruate late; they are apt to have long periods of amenorrhea or suffer from dysmenorrhea. The hypoplasia of the soft part renders defloration difficult, and this in turn may produce vaginismus. If not actually sterile, they may have frequent abortions. Even if pregnancy continues, the minor disturbances of gestation appear in an exaggerated form. The rigidity of the underdeveloped uterine wall renders fetal motions which normally are below the threshold of conception, excessively painful. Cervical and perineal lacerations are the rule, and so are complications on the part of the contracted pelvis. In the puerperium there is a noticeable lack of resistance against loss of blood or infection, and the milk supply is generally insufficient. As such women are very apt to emerge from labor with a pendulous abdomen, enteroptosis and prolapse, it is quite comprehensible that to them the reproductive function represents a veritable *via dolorosa*, and that they strenuously object to having more children.

In clinical gynecology, most of us will have to confess to our failures, and to the unreasonableness, of dilatation or incision of a "pin hole os." Congenital retroflexion, likewise, should be a touch-me-not. "In about one-third of all virginal retroflexions the painstaking observer will find stigmata of infantilism," says A. Mayer whose admirable work is freely quoted in this paper.

The frequent association of infantilism and tuberculosis is of diagnostic and prognostic importance. The same is true of the combination of infantilism and the status thymolymphaticus. The small size of heart and aorta, and the lability of the vasomotor mechanism renders any narcosis or loss of blood in operations very hazardous and may account for many a sudden surgical death.

More frequent and even more distressing than the other two is the combination of infantilism with asthenia. What distinguishes the two types is this that infantilism is underdevelopment of *form* whereas asthenia is underdevelopment of *function* (Mayer).

I cannot leave the subject of infantilism without mentioning that there are quite a few individuals who give the general impression of a pronounced infantilism, yet behave and function in a perfectly normal way. They are invariably far below the average size, look like children, have delicate bony structures and a proportionately small pelvis, and possess a sunny, happy disposition. On careful examination none of the dwarfed primary or secondary sexual characteristics of true infantilism can be detected. They pass through pregnancy, labor, and puerperium without marked difficulties and frequently are even exempt from the usual birth injuries. This group must be regarded as miniature editions of the normal woman and not be confused with the hypoplastic type which has been discussed in the foregoing.

The "intersexual" or masculine type does not seem at first sight to belong in the same category with asthenia and infantilism; for many representatives of this type are above the average in height, and all are characterized by a strong skeletal build and pronounced facial features. The distribution of hair is characteristic. The lower legs, the forearm, the perianal region, the buttocks are covered with hair, and the pubic hair extends from the mons pubis along the linea alba towards the umbilicus in the form of the triangle which is rather typical of males. Frequently, too, the eyebrows meet and there is a more or less faint suggestion of a mustache. In more severe cases, there is hair on chin, thigh, upper arm, back, and breasts. This abnormal hirsutism is the reason why Aschner designates this type as "hypertrichotic."

The shoulders are broader than the pelvis; the latter is, as a rule, of funnel shape and with a greatly reduced inclination, and always there is a free space between the thighs.

The ovarian function is diminished. In consequence, there is often a hypoplasia of the genitals as in infantilism, and frequently a combination with the asthenic hypotonus.

It was Mathes to whom we owe the classical description of this category and the term "intersexual type." He explained its occurrence by the fact that originally the *anlage* of every organism is bisexual and that only at a later stage of development the predominance of one or the other sex gland leads to the determination of masculinity and femininity, respectively. In the type under discussion this differentiation remains incomplete; hence the individual remains intersexual.

Such patients are subject to dysmenorrhea, frigidity, and dyspareunia, symptoms which in the last analysis are due to disturbances of the unstable nervous system. They rarely have complete orgasm; hence, there results a chronic hyperemia of the genital organs (Fekete) which in turn may be responsible for cystic degeneration of the ovaries, menorrhagias, and tender sacrouterine ligaments and thus, finally, to dyspareunia and sterility.

Disturbed ovarian function upsets the equilibrium of the endocrine system which explains other clinical symptoms.

The intersexual individual suffers, consciously or unconsciously, from her physical incompleteness. She may rebel against manifestations and functions of her femininity such as menstruation which appears to her as unaesthetic, or marriage which impresses her as humiliating. On the other hand, she may yearn to be fully a woman and passionately wish for a child which, for physical reasons, is only too often denied her. Her whole life is a sum of physical and mental conflicts. This psychic component has been studied particularly by Kretschmer who classifies these patients among the "schizophrenes." From a gynecologic point of view it is interesting to note that L. Fraenkel and his pupil Geller have found infantilistic genitalia in a large percentage of schizophrenic women; microscopically, there were few follicles in the small ovaries, and the uterine mucosa showed low epithelia and narrow glands without signs of activity.

While in mild forms of intersexualism, happy domestic relations and, particularly, conception and childbirth may bring about a satisfactory solution, the majority of cases have to go through the martyrdom of life as best they can, until in advanced age the disharmonies of the torn personality dissolve themselves spontaneously (Mayer).

The hypertonic category though numerically smaller than either of the other two groups, is composed of several widely different types.

There is, first, the physiologic giantess, that is to say, an individual in whom all the physical characteristics of a normal woman appear in an exaggerated form. Some of Rubens' models represent this sort of super-woman. Her height does not seem as excessive as that of the masculine type, because her body is perfectly proportionate and harmonious; and though her panniculus adiposus is well developed, we call her fleshy rather than stout. One feels that she has an intense joy in living without the usual physical handicaps, and that her large pelvis, exceeding the average measurements by an inch or more in each diameter, safeguards easy labors. Whether the mental development is on a par with the physical, I am unable to tell from my own few observations or the scanty references in literature; but one unconsciously connects Catherine the Great or, perhaps, Catherine de Medici with this type of hypertonus and hyperplasia.

Another kind of gigantism impresses us by its lack of harmony whether this be in the form of a general obesity or, on the contrary, the poor development of adipose tissue. Disturbances on the part of various endocrine glands are here at work, notably the hypophysis and the adrenals. Since such glandular disorders are but very rarely acquired even if they manifest themselves in later life, the constitutional nature of this pathologic gigantism seems definitely established. The chapter of endocrinology has been studied so intensely that we may confine ourselves to a mere mention of acromegaly and other disorders. It is significant to note in this connection that competent observers claim that abnormal obesity is constitutional in the majority of cases. Van Noorden esti-



mates familial incidence of obesity in 70 per cent, Bauer in 88 per cent (Silver and Bauer). "This perversion of metabolism is the work of a *congenital* factor already present in the fertilized ovum, that destines the organism to accumulate fat." This assumption seems to find confirmation in the interesting experiments by Strandberg who transplanted fat from the abdominal wall to the dorsum of the hand. It is known that the back of the hand rarely becomes fat, yet in these cases a distinct, local, unilateral obesity occurred at the site of the transplant. This indicates that the transplanted abdominal wall, though separated from its previous nerve and blood supply, retained its lipophilia, that is, its irresistible tendency to accumulate fat.

As Mayer points out, it is not always easy to differentiate between physiologic and pathologic overgrowth of the body. In general, the "normal" giantess is apt to begin menstruating early, the pathologic giantess late, because in her there is usually a hypofunction of the ovaries demonstrable. Many such giantesses have small hearts; loss of blood in labor or operation, narcosis or infection are, therefore, rather dangerous.

#### UNSOLVED PROBLEMS

I am well aware that the classification of constitutional types presented in the foregoing, is incomplete, that it does not take into account the numerous blendings and variations which occur but cannot easily be put on paper, that it leaves out exceptional cases which seem to fit into no category. But, after all, this classification is only to be a temporary expedient to illustrate this plea for greater consideration of the constitutional factor in gynecology and obstetrics. It will and must be changed as our experience grows and unsolved problems have been cleared up. And there are many such questions that clamor for answer. Why is it, for instance, that certain individuals and certain races show a marked tendency toward formation of keloids? Why, on the other hand, do abdominal incisions sometimes break open completely in the absence of infection or any other tangible cause such as syphilis, cachexia, or advanced age? Fear or excitement may in some women bring on menstruation prematurely or suddenly check an existing one, but has no such effect on others. In pregnancy a slight jarring may lead to bleeding and abortion in one case while in another an automobile trip from coast to coast will not interrupt gestation.\* It is well known that red haired women frequently have a postpartum hemorrhage even though the delivery was spontaneous and skillfully managed. There are, also, instances of famil-

\*Such individual differences have attracted attention for many, many years. In A. E. von Siebold's *Handbuch der Frauenzimmerkrankheiten* (Vienna, 2: 211, 1829) I found the following passage: "Most women who have bleeding spells in pregnancy, have a certain disposition to hemorrhages though the nature of the latter cannot always be determined . . . some women show no effect from even the most severe external traumatism while others bleed abundantly after a very mild injury . . . *weakly, asthenic constitutions* (italics mine), flabbiness and weakness of the uterus preeminently predispose to uterine bleeding." This reference of more than one hundred years ago has been inserted merely for its historical interest. I realize that in explaining obscure phenomena by constitution, we substitute for the unknown factor another unknown or but imperfectly understood quantity.

ial postpartum hemorrhage that can only be interpreted as constitutional. Recently, Embacher reported a striking instance of this kind. The mother had nine normal deliveries, and no obstetric complications were known of in either the maternal or paternal immediate family. The four daughters ranged in age from sixteen to twenty-five years; the pelvic measurements were normal, the deliveries spontaneous, the children healthy, and the placentas showed no abnormalities. Yet, each of these four sisters had a severe postpartum hemorrhage in every one of their confinements.

As a final illustration of unsolved problems of constitution, the occurrence of familial icterus of newborn may be cited. In a personal observation of this kind, the mother, a healthy woman of normal constitution, gave birth to four children; the first, a girl, is alive and well; of the following three, all boys, each died of severe jaundice exactly fifty hours after birth in spite of competent pediatric treatment.

From these few examples which can easily be multiplied, it is seen that our knowledge in this field is still very fragmentary.

#### PRACTICAL ASPECTS OF STUDY OF CONSTITUTION

On the other hand, the study of constitution has already yielded many valuable new viewpoints in gynecology and obstetrics—largely in the sense of diagnosis and prognosis but also, to a certain extent, in the question of therapy.

To choose a few instances at random, we have learned to recognize the constitutional nature of certain cases of dysmenorrhea, frigidity, dyspareunia, and vaginism. Menstrual pain had been considered since the days of Marion Sims, as being due to obstruction at the internal or external os. Today we can admit this etiology only in a very small minority of cases. Hence the multitudinous dilatations and discissions of former years have been substituted by a more causative therapy which aims at reducing the psychic hypersensitiveness and quieting the irritable vegetative nervous system in constitutional inferiority. The surgical enlargement of the vaginal entrance for the cure of vaginism now appears obsolete. Congenital retroflexion is almost always associated with other signs of infantilism and does not call for indiscriminate operation. The complaints of such patients are not caused by any displacement but are due to their constitutional deficiencies, and we cannot hope by surgical means to transform the hyperesthetic organism with its low threshold for any sort of pain or other unpleasant sensation. But even in acquired retroflexion, restraint from operative overzeal is in order. Asthenics quite commonly present a multitude of complaints among which backache, pain in the ileo-inguinal region, sense of weight, dysmenorrhea, and vaginal discharge are conspicuous. On examination, only insignificant findings are, as a rule, elicited. Thoughtful surgeons have long warned against the routine removal of the so-called "chronic"

appendix in such cases. Gynecologists, too, are beginning to weigh cause and effect more carefully. Operation for the uterine displacement alone will at best yield but a temporary improvement. What these patients are most in need of is rest in bed, a high caloric diet, treatment of constipation, some passive exercises, and a suitable support. Only if there are anatomical changes in the retroflexed uterus as evidenced by menorrhagias, or if the displacement is associated with prolapse, is surgical therapy clearly indicated.

There are cases where this new appreciation of constitutional factors makes us recognize our own therapeutic limitations more keenly. Thus, in an adult woman of a marked intersexual type we are forced to realize that her gynecologic complaints are not amenable to any gynecologic treatment. Patients of this sort should be referred to a neurologist for psychotherapy so that they may be tided over until the menopause automatically makes an end to their psychical conflicts and physical complaints.

The rôle of constitution in sterility has been made the subject of intensive investigation. Berkow studied 69 sterile women without any physical anomalies in the genital sphere, in whom the Huhner test showed motile spermatozoa; of these 69 patients, all but one were constitutionally abnormal (eunuchoid, obese, infantilistic, etc.) Of the 25 cases investigated by Meaker, almost one-fourth failed to conceive for reasons of faulty constitution.

Whether or not constitution influences the ordinary disturbances of pregnancy, is still undecided. It seems, however, that hyperemesis occurs more frequently in asthenics. Primary inertia has, of course, various causes; yet, it is observed most often in infantilistic and asthenic women who at the same time are refractory to pituitary extracts and other oxytocics. It is, therefore, not surprising that in this class of patients confinements as a rule, are harder (Givatoff), particularly if one also takes the condition of pelvis and pelvic floor into consideration. Isaksohn found rupture of membranes before onset of labor in 35 per cent of asthenics and none in normal women; duration of first labor of more than 24 hours was noted in 20 per cent of normal and 50 per cent of asthenic patients.

Eclampsia seems to be the only complication in pregnancy which shows a predilection for the normal type. The patients are as a rule primiparae and below thirty years of age, and almost always well nourished, florid, stocky women which makes one suspect a relationship between this form of toxemia and constitution.

Such differences in susceptibility to disease have often been noted. It is, for instance, generally accepted that hypotonics are unduly susceptible to tuberculosis while the normal type shows a propensity to cancer. Regarding cancer, the view now prevails that it is a local disease which, however, is based on a constitutional disposition (A. Fraenkel). From

a thorough analysis of 858 cases, Benedetti concludes that cancer prefers the so-called constitutional and physiologic optimum; and among the 81 patients with cancer of the uterus studied by Takata and Suzue, almost all exhibited a "strong" constitution with a costal angle of more than 90 degrees.

Other differences in liability to disease have been mentioned in the body of this paper. I refer in particular to the dangers from narcosis, hemorrhage and infection to which some types are more exposed than others. In a thoughtful paper on predestination in disease, W. Langdon Brown discusses variations in proclivity to disease based on inborn errors of metabolism, idiosyncrasies, endocrine balance, factors which are intimately connected with our subject, yet had to be curtailed for lack of time and space. Here, too, may be mentioned in passing Aschner's contention that the complexion has a great deal to do with individual reactions. Blond persons have a much more sensitive skin to sunlight, x-rays, counterirritants, etc., than dark ones. A laxative which acts only mildly on the latter, is a purge for the light skinned. Aschner points out that the old physicians knew that the pigmentation of the skin is a criterion of the "humors" beneath. For instance, the milk of blondes is less concentrated than that of brunettes.

The study of constitution permits us to a certain extent to predict the course of the climacterium. The perfectly normal woman "glides, as it were, insensibly, from the reproductive age into the menopause, practically without any physical or psychological upheavals" (Wiesel).

In the woman of the intersexual type the change of life imposes new hardships: severe vasomotor disturbances, all sorts of "nervous" symptoms, insomnia, depression alternating with excitement, vertigo, gastrointestinal upsets, pain along the course of vessels. This sort of patient is likely to lose weight, in contrast to the normal woman who is apt to become stout, and to exhibit markedly masculine traits (hair on face, deep voice, etc.)

The infantilistic patient with a pronounced hypoplasia of her endocrines need not have any change of life in the strict sense of the word. Her development has remained arrested all her life.

The asthenic individual is likely to suffer severely during this epoch. All symptoms due to her ptosis become aggravated, the constipation is more obstinate, abnormal and painful accumulation of fat may interfere with locomotion, and all this distress is quite apt to continue for years.

Knowledge of the constitution of the patient will furnish us with certain valuable hints in our practical work. It will stay our hands from a number of unnecessary operations. It will also lead us to better technical methods in operating. The most impressive example is prolapse in children or nulliparous women. Most patients of this sort are infantilistic asthenics. They have a hypoplasia and weakness of all the tissues of the pelvic floor and the ligaments of the uterus. The lack

of firmness, elasticity and resistance of the connective tissue fibers explains the frequent failure of the ordinary type of prolapse operations in these cases (Offergeld). Even more important, however, is the abnormal depth of the culdesac which in infantilistics, extends all the way down to the pelvic floor. Therefore, only a method which provides for a complete obliteration of the culdesac, promises permanent result in this class of cases.

Appreciation of constitutional influences also helps us to prevent gynecologic ailments. We may, for illustration, once more refer to prolapse in hypotonics. Knowing beforehand the flabbiness of all structures in such patients, we would pay particular attention to a prenatal régime of good feeding and graded exercise and give even greater care to these points after the birth of the child. These patients must rest in bed longer than others and take systematic and supervised exercises of the muscles of the pelvic floor and abdomen. In labor they must be guarded against unnecessary exertion, pain, and undue prolongation of the second stage by means of "twilight sleep," local or general anesthesia, and a liberal use of episiotomies and low forceps. In the puerperium they should not be allowed to nurse, lest there result a lactation atrophy which might become permanent and lead to sterility. The use of a suitable corset or abdominal support is of great importance.

#### TREATMENT OF CONSTITUTIONAL INFERIORITY

Is it possible to affect therapeutically a constitution which is inimical to the patient's health? To a certain extent, yes. Some infantile uteri may grow after marriage, and some dysmenorrheas may disappear (Mayer). Perhaps, organotherapy, despite its present disappointing results, may yet improve matters if instituted sufficiently early in life. Several personal observations have somewhat restored my optimism. As endemic myxedema points to the influence of soil and water, as change of occupation sometimes depresses ovarian action and tropical climate often stimulates it, we are led to hope that we may accomplish results by changing the environment. Nor should we forget the possibilities which diathermy and other means of inducing local hyperemia offer as to the growth of the genital organs.

An asthenic, thin, hypotonic individual can be rendered much stronger and more resistant by such drugs as iron and arsenic, by stimulating her appetite and increasing her body weight, by hydrotherapy, by ocean baths or, on the contrary, by the stimulation of altitude. The sovereign therapy, however, is muscular exercise both active and passive, systematically graded and suited to the individual needs (Goldscheider), and the avoidance of harmful influences (alcohol, tobacco, infections, trauma, excessive emotions, physical and mental overwork). In the constitutionally obese, on the other hand, dietary and pharmacologic treatment (iodine, mercury, thyroid extract, saline purgatives), to which Aschner adds the use of venesection, are in order. "Thus many

cases of obesity associated with scanty menstruation, sterility or climacteric disturbances can be improved or even cured'' (Aschner).

Sometimes pregnancy produces a spontaneous cure of infantilism, and one is delighted to see that such women positively blossom out.

#### PREVENTION OF CONSTITUTIONAL DEGENERACY

Much more important than the therapy of inferior constitutions is their prophylaxis. We must bear in mind that the law of natural selection no longer applies universally to mankind, and that civilization tends to preserve the unfit. Something should be done to check the endless stream of these ill adapted individuals and to improve the constitutional quality of the race. Borchardt's contention that persons with particularly undesirable congenital features should not be permitted to propagate, and that in less severe cases one should at least see to it that the sexual partner does not exhibit the same stigmata, will very likely remain a pious wish. Yet, there is a wide and promising field for preventive measures. An encouraging beginning has already been made in our prenatal care in which, I believe, this country has taken the leading part. If prenatal care were universal and uniformly thorough, the total abolition of congenital syphilis with its deleterious effect on the constitution of the offspring is quite conceivable. Neither does it seem altogether fanciful to imagine that the baneful influence of lead, alcohol and other poisons on the parental gonads can be eliminated, or at least restricted, with increasing enlightenment of the people. Other factors leading to a constitutional improvement of coming generations will no doubt be evolved. The experiments by Freund and Schmitt appear to me highly suggestive. These authors exposed 229 pregnant women to ultraviolet radiation and contrasted their offspring with the children of 222 "unradiated" mothers. They found that the children of the first group were a little longer and heavier than those of the second group, that they less often developed rachitis and presented a higher phosphate level in the blood. Better obstetrics, generally speaking, will avoid many of the harmful influences which act upon the constitution at the time of birth. "The present generation of grandparents and parents is beyond our control so far as prophylaxis is concerned. Not so, however, with the grandparents and parents of future generations" (McCurdy).

Nor must our vigilance cease after the child is born. In our introductory remarks we have included in our definition of Constitution the environmental factors which may act unfavorably upon the hereditary traits of an individual. As W. Langdon Brown expresses it, the seed is not all-important . . . the soil must also be considered. A multitude of hygienic deficiencies may affect the growing child, and, according to Hering, *everything* that happens to an organism during its life, leaves ineradicable traces in the memory of the matter. It is no mere accident that the children of the proletariat in crowded tenements

are shorter in stature than those of more privileged classes, just as a lack of fundamental hygiene was probably responsible for the shorter growth of man in the middle ages as anyone knows who has seen medieval armor in Continental museums.

Fortunately there are nowadays in addition to individual endeavor many social agencies capable of utilization in the solution of this problem. The juvenile courts, playgrounds, recreation centers, home-finding agencies, fresh-air farms, etc., are all important and valuable measures.

"It is only through a great public awakening to the fact that every child, rich or poor, has an inherent right to that individual care which will develop his potentialities to their highest point that we can hope to make material progress. This awakening must come through the physician. It is he alone who is capable of understanding the complex make-up of the child and the significance of apparent deviations from the normal. It should be his province to direct the detail of those environmental influences which make or mar the future; this with normal children, as a preventative of hypoplasia, and, with hypoplastic children, that the tendency to further degeneracy may not only be arrested but that regeneration may be encouraged" (McCurdy).

#### CONCLUSIONS

A short survey of any intricate subject necessarily remains sketchy. Thoroughness has to yield to brevity. But certain general facts and principles emerge clearly.

We started out to study the constitutional factor in gynecology and obstetrics and we found that this study involved questions connected with anthropology and embryology, pharmacology, biochemistry and clinical medicine, pathology and eugenics. With so many links connecting gynecology and obstetrics with all the other fields of medical endeavor, there can no longer be talk or fear lest specialization lose its contact with the general science of Medicine from which ours as well as every other specialty has sprung.

Medical science, again is not an isolated phenomenon but, as Seelig aptly says, "the development of medical thought and medical activity in any country, or during any era, is only a reflection of the general culture, mode of thought, habits and general reaction to environment on the part of the people under consideration."

The study of constitution, therefore, accomplishes two results of great general import: it links our specialty once more with Mother Medicine and establishes our place as gynecologists in the life of the nation.

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METROPOLITAN BUILDING.

## PELVIC ENDOMETRIOSIS AND (TUBAL) FIMBRIAE\*

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**A**DENOMYOMA, adenomyosis, endometrioma, müllerianoma, endometriosis, müllerianosis and endosalpingiosis are a few of the names which have been introduced by various writers to indicate misplaced müllerian mucosa (of uterine or tubal type) in or upon the pelvic structures. In some instances this ectopic tissue can be shown to have arisen by direct extension from the mucosa lining the uterus or tubes, but more often its origin is due to some other phenomenon. In the majority of the latter cases, implantation-like patches of müllerian mucosa are present on the surface of the various pelvic structures, often with a varying degree of invasion of their host. Although peritoneal endometriosis can occur without an associated ovarian endometriosis (including endometrial cysts of that organ), more often both conditions are present in the same individual.

It is the purpose of this communication to consider the following phases of pelvic endometriosis:

1. The structural similarity between peritoneal endometriosis and peritoneal carcinomatosis of ovarian origin, suggesting a like development of the two conditions.
2. The relation between ovarian and peritoneal endometriosis.
3. The indications: (a) that frequently müllerian mucosa on the surface of the ovaries and peritoneum is primarily, in part, the result of a

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local reaction to some substance escaping into the pelvic cavity from or through the patent tubes; (b) that this substance is in solid form and (c) that menstrual blood is one cause of this reaction and therefore contains this substance.

4. The evidence that the müllerian mucosa on the surface of the ovaries and peritoneum, caused by some substance escaping through the tubes, may arise entirely from a differentiation of tissue "in situ."

5. The evidence that the foreign substance (cells) causing the local reactions on the surface of the ovary and peritoneum is derived from müllerian mucosa and is sometimes held captive in the scar of the wound caused by them and there continues to grow, as cancer cells grow when implanted in these situations.

In the life history of pelvic endometriosis it is natural to consider the part taken by the mucosa of the uterus and the tubes especially that of the tubal fimbriae since they lie exposed in the pelvic cavity when the tubes are patent, the tubes usually being patent in patients with pelvic endometriosis.

During the study of tubal fimbriae a form of fimbrial endometriosis was found which apparently arose from a differentiation of their mucosa into endometrium-like tissue. To this condition the name *primary fimbrial endometriosis* might be given. This differentiated and activated mucosa may invade the wall of the tube, the mesosalpinx and also by direct extension reach the surface of the ovary and even cause endometrial cysts of that organ. By its reaction to menstruation, fragments of müllerian mucosa are disseminated into the pelvic cavity. Therefore the menstruating mucosae of primary fimbrial endometriosis are active foci for the spread of müllerian tissue and may be one cause of misplaced müllerian tissue on the surface of the peritoneum and ovaries, and of endometrial ovarian cysts.

#### THE STRUCTURAL SIMILARITY BETWEEN PERITONEAL ENDOMETRIOSIS AND PERITONEAL CARCINOMATOSIS OF OVARIAN ORIGIN

The proof that cancer invades its host is absolute because this extension of the cancer can be definitely demonstrated. In like manner uterine and tubal epithelium, at times, invades the uterine and tubal walls, thus giving undebatable evidence as to the source of the ectopic müllerian mucosa in these cases.

When a "secondary" cancer is found, which can be shown not to be continuous with the assumed primary tumor it may or may not have arisen from the growth of cells transported from the primary cancer through well-recognized channels. The chain of evidence, indicating that secondary cancer is ever of metastatic origin, is broken and therefore this evidence is at best circumstantial. The same is true for the origin of misplaced müllerian mucosa not continuous with that lining the uterus and tube.

A study<sup>1</sup> of the lesions of the peritoneal carcinomatosis so often associated with ovarian carcinoma, demonstrates that the majority of them apparently arise from the repair of injuries to the peritoneum caused by cancer cells which had escaped into the peritoneal cavity and lodged on the surface of its serous membrane, together with the continued growth of these cells in this situation. The life history of these carcinomatous implants may be divided into the following stages.

1. The escape of cancer cells into the peritoneal cavity from the ovarian tumor.
2. The transportation of these cells to their site of implantation.
3. The reaction of the peritoneum injured by cancer cells lodging on its surface.
  - (a) Fixation of the cancer cells by fibrin.
  - (b) Organization of the fibrin by fibroblasts alone, or by both fibroblasts and vascular endothelium forming granulation tissue.
  - (c) Transformation of the organized fibrin into connective tissue.

The form of the implant varies with its age, the reaction of the peritoneum to the injury, and the activity of the cancer cells. The mature implant may consist of cancer cells embedded in the thickened peritoneum or encapsulated on its surface. In other instances it resembles a polyp wholly or partially encapsulated. The polyp may be sessile or pedunculated. Implantations in adhesions frequently occur. All the implantations just described may be designated as those of the foreign body type.

There is one form of peritoneal cancer found in patients with peritoneal carcinomatosis, associated with ovarian cancer, for which a true metastatic origin might be questioned; that is, the uncovered or non-embedded tumor which is attached to or spreads over the surface of the peritoneum like a primary growth arising from the mesothelium in this situation. Since the mesothelium and the cells of the ovary in which the cancer arose, undoubtedly had a common ancestor, i. e., the celomic epithelium, it might be inferred that whatever causes a differentiation of ovarian epithelium into cancer might effect a like differentiation of its closely related peritoneal mesothelium. This would be an example of the multicentric origin of cancer in closely related structures, well recognized by pathologists and recently stressed by Robinson<sup>2</sup> in his discussion of the origin of primary and secondary ovarian cancers. If this type of peritoneal cancer is in any way related to the ovarian tumor it might be claimed that it arose from the stimulation of the mesothelium by some substance escaping from that tumor into the peritoneal cavity. On the other hand, the cancer cells might be grafted on the surface of the peritoneum like small skin grafts or the cells may have been covered with fibrin which did not become organized and therefore disappears. For these reasons I have been tempted to consider at least some instances of this form of peritoneal cancer as implantations of the skin graft type.

We have abundant proof that cells may escape into the peritoneal cavity from the ovaries, tubes and even the uterus. What happens to them? Are they all absorbed without any evidence of a peritoneal re-

action? The distribution of the pelvic peritoneal lesions of endometriosis is such as to indicate the possibility of their origin from the above mentioned sources. The reaction of the peritoneum is often similar to that stimulated by foreign material lodging on its surface. Various stages in this reaction may be found corresponding to those encountered in the embedding or encapsulation of foreign bodies introduced into the peritoneal cavity of lower animals and in the implantation of cancer in human beings. Therefore, the deposits of müllerian mucosa on the surface of the peritoneum often present exact counterparts of the embedded implants of cancer just described, except that the cancer cells are replaced by müllerian epithelium and often the stroma by müllerian stroma. In other instances the müllerian mucosa is attached to or spreads over the surface of the peritoneum like a primary growth which might have arisen from a differentiation of the mesothelium. These lesions are similar to the uncovered deposits of cancer on the peritoneum which were designated as possible implantations of the skin graft type.

Do the implantation-like lesions of peritoneal endometriosis represent localized metaplasias of the peritoneum caused by some specific stimulant escaping into the peritoneal cavity from the ovaries, tubes or uterus, or are they the result of the repair of injuries caused by cells, escaping from the above-mentioned sources, which lodged on the surface of the peritoneum and there continued to grow in the way we believe peritoneal carcinomatosis may often arise? Have all implantation-like patches of pelvic endometriosis a similar origin? Are some derived entirely from a metaplasia or differentiation of tissue "in situ," and others from a local reaction along with the retention and growth of transplanted cells? It is obvious that these questions cannot be answered to the entire satisfaction of all, any more than can similar questions in regard to the origin of peritoneal carcinomatosis. It is quite possible that in both instances some of the peritoneal lesions may have arisen from the embedding or grafting of transported cells and others from a differentiation of tissue "in situ." A comparative study of peritoneal endometriosis and peritoneal carcinomatosis must convince one that the peritoneal lesions in the two conditions often have a similar origin.

#### THE RELATION BETWEEN OVARIAN AND PERITONEAL ENDOMETRIOSIS

Ovarian endometriosis may be divided into three groups.

1. Müllerian-like mucosa on the surface of the ovary, often invading that organ, without the presence of an endometrial cyst or a hematoma.
2. Endometrial cysts wholly or partly lined by tissue of the histologic structure of müllerian mucosa, often with similar mucosa on the surface of the ovary. I believe this group often represents a later stage of the preceding one.
3. Hematomas in which typical müllerian-like mucosa is lacking in their lining. I have hesitated to classify any of these hematomas as müllerian (endometrial) unless they were adherent and there was evidence of a previous rupture or perforation and endometriosis was present in the structures adherent to the ovary at the site of the perforation of the hematoma.

In the first two of these three groups there is nearly always (if not always) an associated peritoneal endometriosis. It is obvious that the ovarian and peritoneal endometriosis in these cases must either have a common origin or else one is derived from the other. It also must be obvious that some of the peritoneal endometriosis found in the second group was probably present before the ovarian hematomas had developed and therefore did not entirely arise from the rupture of the latter. Observations made at operation, together with the microscopic examination of tissue removed, demonstrate that müllerian mucosa on the surface of the ovary and likewise lining these cysts may, by direct extension invade adherent structures and that the contents of these cysts at times escape into the pelvic cavity. All stages in the rupture of these cysts and the repair of the resulting injury have been observed at operation. One is convinced therefore that at least some of the adhesions present in these cases arise from the escape of the contents of the hematomas and the repair or closure of the perforation. The presence of müllerian mucosa in these adhesions, as well as the distribution of other peritoneal foci, speak for the origin of at least some of these lesions from the contents of the ovarian hematoma escaping into the peritoneal cavity.

In a paper published by me<sup>3</sup> in 1921, on hemorrhagic cysts of the ovary and their associated peritoneal adenomas of endometrial type, the origin of the adenomas was regarded as derived from menstrual blood escaping from the perforation of the ovarian hematomas and likewise from endometrial tissue on the surface of the ovaries. Both the metaplasia and implantation theories were considered in the discussion of the development of the peritoneal lesions from this source. Up to that time I had not attempted to determine the origin of the müllerian mucosa (including the hemorrhagic cysts) in the ovary, but believed that the principal, if not the sole cause of the peritoneal endometriosis in these cases, was the implantation of epithelium carried with the contents of the ovarian hematoma escaping into the pelvic cavity or conveyed with menstrual blood from the endometrial tissue on the surface of the ovary.

King,<sup>4</sup> in a recent paper on the origin of endometriosis of the ovary and its associated peritoneal endometriosis, states that the lining of the ovarian cysts "arises probably by metaplasia from cells which are present in the ovary and not from cells of another organ by a peculiar process of transplantation." He believes that the peritoneal lesions "are produced, in almost every case, by the implantation of epithelium from tarry cysts."

Novak,<sup>5</sup> in a recent paper on pelvic endometriosis, made the following statements in his summary of its etiology and histogenesis. "The celomic heteroplasia theory explains the lesions more logically and has wider applicability than any other, in so far as the actual cause is concerned, but that implantation must, almost certainly, play a part in the dissemination of the process once it has begun" . . . "In other words, I do not believe that endometrial cysts are the result of implantation of tissue carried from the uterus through the tubes at menstruation, but rather that some other factor brings about the further differentiation of germinal epithelium into endometrium" . . . "On the other hand, once endometrial cysts have developed in the ovary, their frequent perforation, with the setting-free of tissue which in this

case may be viable, together with the direct invasive growth of endometrium into adherent tissues, would seem to offer a logical explanation for the common clinical pictures found." In discussing the perforative tendency of endometrial cysts, Novak states, "The physiologic hemorrhage which takes place from the endometrial lining of the cysts at the menstrual periods would seem to offer the logical explanation for this perforative tendency associated as it must be with an increased tension of the cyst contents."

It is evident that Novak believes, as I do, that tissue set free by the menstrual reaction in the endometrial lining of these ovarian cysts, is sometimes *viable* and escaping into the pelvic cavity may become implanted on the peritoneum. Why should not similar tissue, set free by the menstrual reaction of endometrial mucosa in other situations also sometimes be *viable* and capable of becoming implanted on the peritoneum, or even on the surface of the ovary, should it escape into the pelvic cavity? I still believe, as I did in 1921, that peritoneal implantations frequently arise from endometrial tissue in the ovary (including endometrial cysts) and by later studies I am convinced that they may result also from the menstrual reaction of endometrial tissue on the surface of pelvic organs and structures other than the ovary, and likewise from tissue escaping from or through the patent tubes. Peritoneal endometriosis frequently occurs without demonstrable müllerian mucosa in the ovaries as will be discussed later. Therefore the peritoneal endometriosis associated with endometriosis of the ovary may or may not have been entirely derived from the müllerian mucosa in that organ.

#### PATENCY OF THE FALLOPIAN TUBES AS A FACTOR IN THE ETIOLOGY OF MÜLLERIAN MUCOSA ON THE SURFACE OF THE OVARIES AND PERITONEUM

With an increasing ability to recognize the early peritoneal lesions at operation, I soon realized that they frequently occurred without demonstrable müllerian-like tissue in the ovaries. I naturally looked for some possible source other than the ovaries, from which material capable of causing peritoneal endometriosis might escape into the peritoneal cavity.

The distribution of the peritoneal lesions was carefully noted at operation, and at the same time observations were made of the normal relation of the fimbriated ends of the tubes to the ovaries and other pelvic structures. The early ovarian lesions were found almost exclusively on the lateral and under surfaces of that organ, situations more favorable than the mesial surface of the ovary for the retention of any solid material escaping from the patent tubes.

In the cases of peritoneal endometriosis without demonstrable müllerian tissue in the ovaries, the distribution of the peritoneal lesions occurred in situations easily soiled by material which might have escaped from the patent tubes, and occurred especially in the natural peritoneal pockets or folds.

I was impressed then, as I now am, with one outstanding feature of patients with müllerian-like tissue within or on the surface of the ovaries, and on the peritoneum, and that is, the tubes are usually patent. Up to

1922 I had studied the conditions found in 71 patients with implantation-like lesions of müllerian tissue on the peritoneum. Fifty-six of these were associated with ovarian hematomas. The abdominal ostia of the tubes in all of these cases were apparently patent. In fourteen of the others the tubes also were seemingly pervious. In the remaining one case, bilateral hematosalpinx was present with a peritoneal lesion on the posterior surface of the uterus in close proximity to the occluded end of the adherent left tube, thus suggesting an intimate relation between the two.

At that time an opportunity was afforded for the microscopic examination of more material. An attempt was made to ascertain the exact structure of the müllerian mucosa in the ovary and peritoneum as a possible indication of its source. It was found that the müllerian-like mucosa in the peritoneal and ovarian lesions, including the lining of the ovarian hematomas, could be divided into three histologic groups, those resembling tubal mucosa, those lined by or containing "uterine mucosa" and a third group containing both tubal and uterine mucosa which I believed might have arisen either from the implantation of both tubal and uterine epithelium or might have represented a transition from one type to the other. A fuller presentation of the data just briefly given may be found in the paper published<sup>6</sup> in 1922.

Patent tubes play an important rôle in the etiology of misplaced müllerian mucosa on the ovaries and peritoneum and therefore it must be due to something escaping from or through the tubes into the peritoneal cavity, which is capable of causing patches of müllerian mucosa in these situations either from a differentiation of tissue "in situ" or from the implantation of tissue (including epithelium) derived from the uterine and tubal mucosa.

THE ORIGIN OF MÜLLERIAN MUCOSA ON THE SURFACE OF THE OVARIES AND PERITONEUM FROM A DIFFERENTIATION OF THE GERMINAL EPITHELIUM AND OF THE MESOTHELIUM CAUSED BY SOME SPECIFIC STIMULANT ESCAPING FROM OR THROUGH THE PATENT TUBES

In 1906 Taussig<sup>7</sup> published a very interesting paper on ectopic decidua formation. He believed that it did not arise in misplaced müllerian tissue, but that it was the result of a local irritation caused by substances escaping from the placenta through the lumina of the tubes. He called attention to the superficial character of these lesions which suggested a surface irritation, and also noted their distribution. They occurred with the greatest regularity on the surface of the ovary, on the peritoneum of the culdesac and that covering the rectum and the posterior surface of the uterus. Because the decidua occurred in patches he believed that the stimulant was not in solution but consisted of cellular detritus. From my own study of ectopic decidua I am convinced that some of them are due to a decidual reaction in misplaced müllerian mucosa present prior to the pregnancy. Granted that Taussig's theory

is correct in many instances, as well it may be, the following deduction might be made from it, which may have a bearing on the etiology of pelvic endometriosis. If ectopic decidua in the peritoneum sometimes arises from the specific stimulation of its mesenchymal tissue by cellular detritus escaping through the tubes of the pregnant uterus, then peritoneal endometriosis might sometimes arise from the specific stimulation of the peritoneal mesothelium by cellular detritus escaping through the tubes of the nonpregnant uterus. There is such a marked similarity in both the distribution and the general character of the two peritoneal lesions that a similar origin might be considered.

During my entire study of endometriosis I have constantly considered its possible development from the specific stimulation of tissue "in situ" as well as its origin from the reaction due to epithelium lodging and subsequently growing on the surface of the peritoneum. The former phase of the subject was discussed in my first paper<sup>3</sup> on the etiology of peritoneal endometriosis associated with endometrial cysts of the ovary, published in 1921, and was again presented in 1926. In the latter paper<sup>8</sup> emphasis was laid on the etiology of pelvic endometriosis from menstrual blood escaping from or through the tubes as well as from endometrial tissue in the ovaries and other pelvic structures. Reasons were given for believing that, if pelvic endometriosis arose from the specific stimulation of the mesothelium by some substance in menstrual blood, this substance must be in solid form, rather than that there were scattered throughout the pelvic peritoneum patches of potential müllerian tissue, which, under the specific action of menstrual blood, developed into müllerian mucosa.

In 1928 Novak and Everett,<sup>9</sup> as a result of their study of the cyclical and other variations in tubal epithelium, made the following statements in regard to the nature and significance of the tubal "secretion." "That this peculiar cellular 'secretion' of the tube, some of which may readily enter the peritoneal cavity, may in some way be related with the etiology of endometriosis." "There is much difference of opinion as to the correctness of the menstrual regurgitation theory of the causation of endometriosis but the fact that the tubes are commonly patent lends much weight to the view that, whatever the cause may be, an important factor must be some substance derived from these open tubes." In the same paper they described an interesting phenomenon, i. e., the extrusion of nuclei from the secretory cells into the lumen of the tube during the premenstrual stage of the menstrual cycle. They state that this is seen in many lower animals but its significance is not known. I had seen these clumps of nuclei in the lumen of tubes, but did not appreciate their origin until Novak and Everett presented their paper. It, then, occurred to me that these extruded nuclei might readily escape into the peritoneal cavity and might even be viable and capable of becoming implanted on the surface of the ovary and peritoneum of human beings, or they might be one of the specific solid stimulants causing a differentiation of germinal epithelium and peritoneal mesothelium into müllerian mucosa.

The following year Hofbauer,<sup>10</sup> in a paper on the etiology of decidua formation in the peritoneum during pregnancy, called attention to the marked resemblance which exists between the topographic distribution of ectopic decidua and endometriosis. He was inclined to favor the theory that, "given the proper stimulus, the

local peritoneal elements, both mesothelial and mesenchymal may possibly take some part in the formation of ectopic endometrial tissue." "This stimulus according to Cunningham may be the presence of blood." "It is common knowledge that a reflux of menstrual blood through the tubes into the pelvic cavity occurs not infrequently." "This blood may be the etiologic element involved in that stimulation of the mesothelium and mesenchyma which results in endometriosis in some instances."

I have purposely studied the peritoneal changes resulting from the escape of blood into the peritoneal cavity during tubal pregnancy. While I encountered many interesting peritoneal reactions I have never observed any simulating peritoneal endometriosis. I have also carefully looked for peritoneal endometriosis in patients who have previously been operated upon for tubal pregnancy and have not seen any except post-operative endosalpingiosis about the tubal stump.

Novak<sup>5</sup> in his recent article on pelvic endometriosis discusses the possible stimuli causing the further differentiation of such tissues as the germinal epithelium or the pelvic peritoneum into actual endometrium. He states that "presumably they are chiefly of endocrine nature." "The only other explanation would be that an adventitious factor is added by some substance emanating from the ends of the tube." "Whether this is menstrual blood or whether, perhaps, it is something secreted by the so-called secretory cells of the tubes, is of course a matter of speculation only in the present stage of our knowledge."

Certainly many of the patches of müllerian mucosa on the surface of the ovaries and peritoneum suggest an origin due to the differentiation of the germinal epithelium and mesothelium into müllerian mucosa just as deposits of cancer in these situations sometimes suggest such an origin. The only other explanation for these uncovered deposits of müllerian mucosa and cancer in these situations is that they are implantations of the skin graft type as has been discussed.

From my studies of pelvic endometriosis I am quite convinced that the stroma is often derived from the tissues of the organ or structure invaded by the müllerian epithelium. If mesenchymal tissue can be converted into müllerian stroma by the presence of müllerian epithelium, why should it not be possible to convert mesothelium into müllerian epithelium by a specific stimulant?

In endosalpingiosis<sup>11, 12</sup> arising from the outgrowth of the tubal mucosa, in the healing of tubal stumps, the activated and often differentiated mucosa may give rise to typical endometrial cysts of the ovary (5 cases) and also typical endometrial tissue in the abdominal wall or any other structure adherent to the stump. As will be shown later in this paper, the mucosa of tubal fimbriae at times becomes differentiated and activated, causing lesions including endometrial cysts of the ovary similar to those arising from the activated mucosa of the tubal stump. A like differentiation of tubal mucosa occasionally occurs in other situations than the fimbriae and in endosalpingiosis of nonoperative origin.

If tubal mucosa under certain conditions is converted into müllerian mucosa of uterine type one might infer that mesothelium, another



derivative of the celomic epithelium, could become differentiated into either uterine or tubal mucosa if given the proper stimulant.

It is evident that abundant circumstantial evidence has been presented indicating that pelvic endometriosis may sometimes arise from the stimulation of the tissues of the surface of the ovaries and peritoneum by some substance escaping from or through the patent tubes during the menstrual life of women. Also there is like evidence that this substance is frequently present in menstrual blood and is in solid form.

#### THE ORIGIN OF MÜLLERIAN MUCOSA ON THE SURFACE OF THE OVARIES AND PERITONEUM FROM THE IMPLANTATION OF EPITHELIUM ESCAPING FROM OR THROUGH THE PATENT TUBES

Since peritoneal endometriosis may occur without ovarian endometriosis, the former is not always secondary to the latter. When the two occur together, they may be identical in their histologic structure and apparently of the same age thus suggesting that they may have had a common origin in these cases.

There is strong circumstantial evidence that the müllerian mucosa in the two situations frequently arises from the actual implantation of epithelium escaping from or through the patent tubes.

1. As has already been presented these lesions seem frequently to arise from some substance escaping from or through the tubes.

2. The histologic structure of the ectopic mucosa caused by this substance escaping from the tubes is the same as that of the mucosa from which the substance was derived, just as the histologic structure of the lesions of peritoneal carcinomatosis is the same as that of the primary growth.

3. Since this substance is evidently often in solid form, it must consist either of cells or of cellular "detritus."

4. The general histologic structure of these patches of müllerian mucosa simulates those of peritoneal carcinomatosis of implantation origin.

5. Bits of müllerian mucosa have been successfully transplanted in the peritoneal cavity of lower animals, reproducing lesions similar to those found in women.

All that is lacking is the proof that epithelium actually escapes from or through the tubes into the peritoneal cavity and that this epithelium is alive and capable of growing when transplanted under suitable conditions. In the study of this phase of the subject one is naturally tempted to assume that the dissemination of tissue from normally situated müllerian mucosa might often be similar to that arising from ectopic müllerian mucosa in the ovary, which we realize is due to the menstrual reaction of this mucosa. Many believe that the tissue disseminated in this manner from the lesions of ovarian endometriosis becomes implanted on the peritoneum and therefore it must have been alive in these instances. It should also, therefore, sometimes be alive when derived through the menstrual reaction of müllerian mucosa in other situations.

About ten years ago I began the study of tubal fimbriae with the hope and even the expectation that the primary source of müllerian mucosa on the surface of the ovaries and peritoneum might frequently be found

in tubal fimbriae. My reasons for this were as follows: I was convinced that müllerian tissue in the ovaries was not responsible for all instances of similar tissue on the surface of the peritoneum. Patent tubes played an important rôle in the etiology of müllerian mucosa both on the surface of the ovaries and peritoneum. In many instances the müllerian mucosa in both situations resembled tubal mucosa more closely than uterine. If derived from tubal mucosa that of the fimbriae would be the most accessible. I had encountered one instance of hematosalpinx associated with peritoneal endometriosis.

The fimbriated portions of tubes were carefully observed at operation. Tubes, after their removal, were placed in a dish of normal saline solution in order to float out the fimbriae which were examined then with a hand lens. I looked for any abnormal conditions, particularly for evidence of the origin of müllerian mucosa on the surfaces of the mesosalpinx and ovary from the invasion of these structures by the mucosa of the ovarian fimbriae and also for endometrium-like changes in the mucosa of any of the fimbriae from which epithelium might be disseminated into the pelvic cavity as from similar tissue in the ovary. At the same time tubes were studied for the presence of endometrium-like changes of the mucosa in situations other than their fimbriae, for indications of tubal menstruation, and also for evidence of a back flow of menstrual blood from the uterine cavity through the lumen of the tubes.

The results of the study of tubal fimbriae were not published because they were not as conclusive as I had wished. However that habit was formed of observing tubal fimbriae at operation and of examining microscopically any abnormal ones. The results of this habit I shall present later in this paper.

On the other hand, the evidence indicating that menstrual blood containing bits of uterine mucosa at times escaped through the tubes into the peritoneal cavity was more conclusive. Blood was observed oozing through the abdominal ostia of the tubes of patients operated upon during their menstrual period. The microscopic examination of sections of the tubes of such patients demonstrated not only blood in the lumen of the tubes but, in some instances, fragments of uterine mucosa. In none of these cases was any evidence found of endometrium-like changes in the tubal mucosa. The papers which were published by me from 1923 to 1927 inclusive dealt with further descriptions of the distribution of ectopic müllerian mucosa and a defense<sup>13, 14</sup> of the theory that metastatic müllerian mucosa could arise from the dissemination of müllerian epithelium set free by the menstrual reaction of this mucosa wherever the latter might be situated and especially from that lining the uterine cavity. The importance of patency of the tubes in the etiology of müllerian mucosa on the surface of the ovary and peritoneum was again emphasized in the papers published during this period. Up to that time (1927) 293 cases of peritoneal endometriosis had been encountered. In 284 of them both tubes were apparently patent. Of the remaining nine

cases, a unilateral hematosalpinx was present in three, bilateral hematosalpinx in two. Attention was called to the possible significance of the relative frequency of hematosalpinx in instances where the fimbriated end of one or both tubes was closed.

As a result of these studies I was convinced that pelvic endometriosis at times arose from the implantation of uterine epithelium carried with menstrual blood escaping from the uterine cavity through the patent tubes. However I was disturbed by two facts. One was the possible significance of hematosalpinx when the tubes were occluded and the other was the tubal type of the mucosa in many of the lesions of pelvic endometriosis, some showing an apparent transition from one müllerian type to the other. In order to understand better this apparent transition the variations in epithelium of known uterine origin were carefully studied: that found in the dilated glands of hyperplasias of the endometrium, that covering submucous myomas, and especially that lining the tubules and spaces of a direct or primary endometriosis (uterine adenomyoma of mucosal origin). Similar studies were made of the variations in tubal epithelium found in hydro- and hematosalpinx and in direct or primary endosalpingiosis (adenomyoma of the tube). From these studies I learned, unfortunately, that the type of epithelium present in misplaced müllerian tissue did not prove its source, and that flattened uterine and tubal epithelium might simulate mesothelium.

During the period of study just mentioned an attempt was made to find endometrium-like changes in the tubal mucosa elsewhere than in the fimbriae and also evidence of tubal menstruation. Many tubes removed during various stages of the menstrual cycle were studied and in not a single instance at that time was uterine mucosa found in the portion of a patent tube distal to the uterus. (Since then I have.) Nor was I able to detect any evidence of a typical menstrual reaction in the mucosa of any of the patent tubes.

A study of the specimens of hematosalpinx and their associated pelvic endometriosis was more productive. I was convinced that the blood in the lumen of these tubes was of menstrual origin and that the associated pelvic endometriosis was probably due to the escape of this blood into the pelvic cavity. In 1922<sup>6</sup> such a case was reported by me, already referred to in this paper. In 1927 a similar case was described in which a patch of typical "menstruating" endometrium-like mucosa was found in the ampulla of the tube (see Fig. 58 of that paper<sup>13</sup>). In three cases of hematosalpinx in which there was not only an associated peritoneal endometriosis, but also a "perforating" hematoma of the ovary, the structure of the epithelial lining of the ovarian hematomas and that of the hematosalpinx was the same.

In 1924 Schwarz and Crossen<sup>15</sup> published the results of their study of "endometrial tissue in the ovary." They described an instance of hematosalpinx with endometrial stroma in its mucosa and evidence suggesting tubal menstruation. In Fig. 16

of that article, a photomicrograph of a portion of an ovary with tubal fimbriae adherent to its surface is shown. In the substance of the ovary glands are present which the authors believe may have been derived from the tubal epithelium in contact with the ovary.

In 1925 Schindler<sup>16</sup> reviewed the literature of adenomyosis of the female pelvic organs and of endometrial changes in the tubal mucosa and likewise reported his own observations. In his conclusions he states that endometrial changes in the tubal mucosa may cause tubal pregnancy and by its participation in menstruation hematosalpinx and possibly misplaced epithelial growths in the abdominal cavity by implantation may result.

Robert Meyer,<sup>17</sup> in 1927, reported three cases with endometrium-like changes in the tubal mucosa. He believes that this condition is rare and of little importance. The same year Lahm<sup>18</sup> discussed tubal menstruation due to endometrial changes in the mucosa and reported one case.

From a review of the literature and my own studies I concluded that mucosa of uterine type in patent tubes is of infrequent occurrence except that found in the intramural portion of the tube from the direct extension of the mucosa lining the uterus. On the other hand, as indicated by the study of hematosalpinx and its associated pelvic endometriosis there is strong circumstantial evidence that tubal menstruation is one cause of pelvic endometriosis.

In 1926 I became greatly interested in the lesions resulting from the healing of salpingectomy stumps as a possible means of obtaining a clue to the etiology of peritoneal endometriosis from tubal mucosa. In salpingectomy operations the surgeon unintentionally cultivates tubal mucosa much in the same way as Jacobsen<sup>19</sup> and others have transplanted successfully müllerian mucosa in the lower animals. The results of the study of the first series of these cases was published<sup>11</sup> in 1928. It was found that frequently "sprouts" grew out from the traumatized mucosa of the tubal stump and invaded the tissue of the stump and any organ or structure adherent to it. The misplaced tubal mucosa arising from this source in some instances retained its original structure, but in others it assumed both the structure and function of the uterine mucosa, including its reaction to menstruation and pregnancy (one case). They presented the histologic picture of the müllerian mucosa found in peritoneal endometriosis of nonoperative origin and of endometrial cysts of the ovary. In that paper three cases of the latter were reported which were shown to have arisen from the invasion of the ovary by tubal mucosa from the adherent stump. (Since then two additional cases of this kind have been encountered.)

In a few of the instances in which "sprouts" were not present, "seedlings" were found in or about the operative wound of the tubal stump which I assumed, in some instances, might have grown from müllerian epithelium transplanted by the surgeon at the first operation. In discussing the bearing of these studies on the etiology of peritoneal endometriosis, including that of endometrium-like tissue on the ovaries and of ovarian hematomas lined by similar tissue, I stated that "many of the

endometrium-like lesions of peritoneal endometriosis could be of tubal and not of uterine origin." "If tubal epithelium transplanted during salpingectomy grows, it should also grow if transplanted during other operations than salpingectomy and by other means than operation." I suggested that tubal epithelium might be transplanted during operations from the handling of tubal fimbriae and that some of the instances of postoperative endometriosis in laparotomy scars after cesarean section might be of tubal and not of uterine origin. I was greatly impressed with the frequency with which the endosalpingiosis of operative origin assumed the structure of the uterine mucosa; much more often, in my experience, than endosalpingiosis of nonoperative origin. While I fully realized that it was not safe to assume the source of misplaced müllerian mucosa from its structure, I was inclined to believe that tubal mucosa played a more important rôle in the etiology of pelvic endometriosis than I had previously thought. Further studies<sup>12</sup> in the healing of salpingectomy wounds confirmed the observations made in the first series and prompted me to study tubal fimbriae more intensely. In 1931 Everett<sup>20</sup> published the results of his study of the type of epithelium present in ectopic müllerian mucosa. I can confirm his observations as to the variation in type of müllerian mucosa found in the lesions of "endometriosis"; that many are of tubal type and that frequently both tubal and uterine mucosa are present in the same specimen, suggesting a transition from one type to the other. This phase of the subject was presented by me<sup>16</sup> in 1922, but not as thoroughly as by Everett. As a result of his studies he believed that pelvic endometriosis is of tubal origin by implantation but did not suggest the mechanism of this phenomenon.

It has been shown that bits of uterine mucosa at times are disseminated through the tubes into the pelvic cavity during menstruation and that sometimes they may be viable. I believe the latter because misplaced müllerian mucosa arises in situations easily soiled by menstrual blood from this source in patients without demonstrable ovarian endometriosis. This belief is strengthened by the evidence that bits of müllerian mucosa disseminated, by menstruation, from müllerian mucosa in the ovary can become implanted on the peritoneum.

The evident relation between hematosalpinx and pelvic endometriosis suggests that the latter might have been derived from the implantation of bits of tubal mucosa disseminated by menstruation from the tubes before the latter became occluded.

As is about to be presented, primary fimbrial endometriosis is a source of endometriosis in other situations both by its invasive faculty and also by the menstrual dissemination of its tissue into the peritoneal cavity.

It is more than a coincidence that the spread of müllerian mucosa from all of the above-mentioned sources should apparently arise from the menstrual dissemination of this tissue.

THE PARTICIPATION OF TUBAL FIMBRIAE IN THE LIFE HISTORY OF PELVIC  
ENDOMETRIOSIS

Should tubal fimbriae take part in the etiology of pelvic endometriosis, the latter must arise either from the direct extension of activated and possibly differentiated fimbrial mucosa over the surface or into the tissues of adjacent structures or from the dissemination of some substance into the pelvic cavity capable of causing patches of müllerian mucosa to appear on the surfaces of the ovaries and peritoneum.

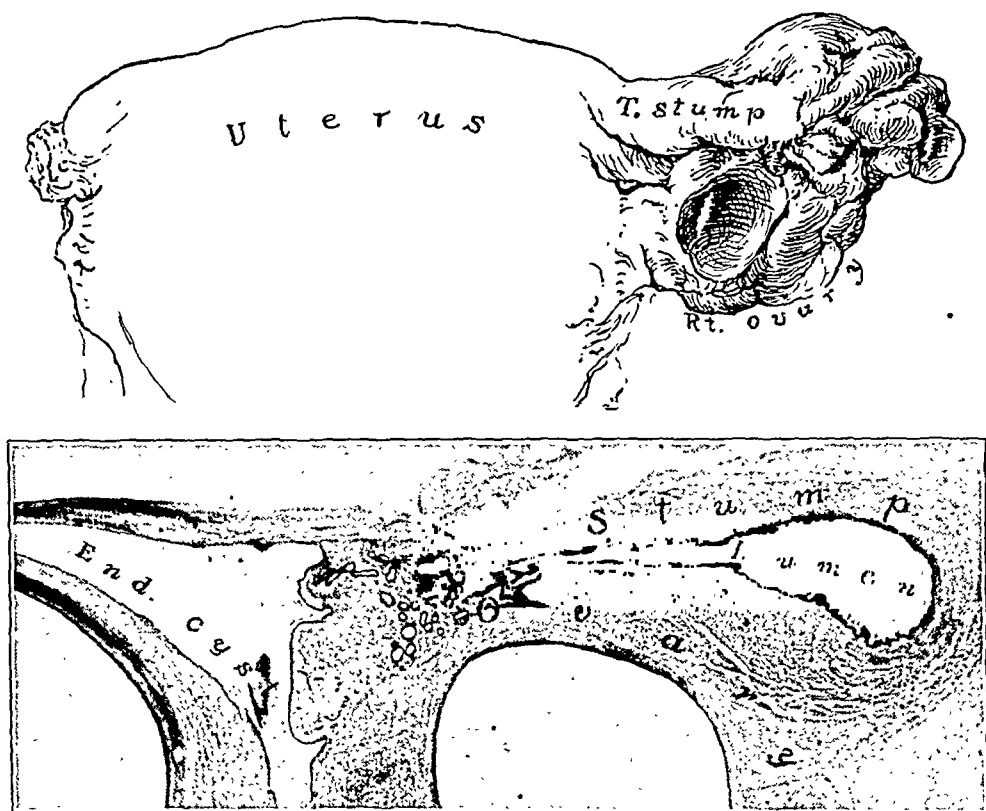


Fig. 1.—A sketch and photomicrograph of an endometrial cyst of the right ovary arising from the invasion of the ovary by the activated mucosa of a tubal stump (see Case 2 of former paper<sup>11</sup>). A previous conservative operation had been done, three years before, for bilateral salpingitis. The sketch shows the tubal stump adherent to and partially embedded in the ovary. Serial cross sections were made of the stump and adherent ovary. The photomicrograph ( $\times 10$ ) shows that the lining of the cyst is continuous with the mucosa of the stump. The stump is lined by typical tubal mucosa but that of the cyst resembles endometrium. This case is one of five encountered, in which an endometrial cyst of the ovary arose from the invasion of the ovary by the activated mucosa of a tubal stump. Many instances<sup>11, 12</sup> were found in which endometriosis developed, in like manner, in other structures which were adherent to a tubal stump. Since the general laws governing the healing of tubal wounds are the same, we would expect that similar conditions might arise in the repair of nonoperative injuries of the tubal fimbriae should such injuries occur.

The rim of the abdominal ostium of the tube is covered by irregular processes, the fimbriae, which vary greatly in shape, size and number. The majority of these consist of a continuation of the mucosa of the tube, often in folds, beyond its ostium. In addition, finger-like projections of the tubal wall are sometimes present—the mural fimbriae—some of which are centrally situated and others are arranged about the periphery

of the mucosal fimbriae somewhat like the sepals of a flower. The extension of the tubal mucosa along the free margin of the mesosalpinx, towards the ovary is known as the ovarian fimbria. These may or may not reach that organ (see Fig. 2).

The line of demarcation between the epithelium of the mucosal fimbriae and the mesothelium of the serosa of the tubal wall follows, in a general way, the bases of the fimbriae but in some instances the tubal epithelium extends beyond this point over the surface of the tube, mesosalpinx and ovary. The central mural fimbriae are entirely covered by tubal epithelium. The palmar surfaces of the peripheral mural fimbriae are covered by tubal epithelium but the dorsal surfaces may be entirely or partly covered by mesothelium, the transition between the two often occurring at the tips of the fimbriae. In all specimens which I have ex-



Fig. 2.—Photomicrograph (x5) of a longitudinal section of the fimbriated end of the tube, the mesosalpinx and a small portion of the ovary. The extension of the mucosa of the tube beyond its abdominal ostium over the free margin of the mesosalpinx to the ovary, thus forming an ovarian fimbria, is well shown. The majority of the fimbriae, in this section, are of the mucosal type, similar to the mucosa of the ampulla of the tube. In a few situations finger-like projections of the underlying tissue are present, thus forming mural or stromal fimbriae. At the mucoserosal junction of mural fimbria "a" the tubal epithelium ends abruptly (see Fig. 3). A similar termination of the tubal mucosa of the ovarian fimbria occurs at the junction of its epithelium with the surface epithelium of the ovary. A cyst-like space lined by epithelium is present at "c" and probably arose from an inclusion of tubal epithelium.

amined, the termination of the epithelial covering of the fimbriae, at its junction with the mesothelium of the serosa of the tube, occurred abruptly, as described by Frank.<sup>21</sup> A similar form of transition is found between the epithelium of ovarian fimbriae, which extend to the ovary, and the germinal epithelium of the latter. This mucoserosal junction apparently constitutes a weak place in the protective covering of the tube and ovary, an area easily stimulated or traumatized and therefore frequently being repaired (see Figs. 3, 4, and 5). This feature may have a bearing on the relative frequency of the development of endometriosis in this situation as will be discussed later.

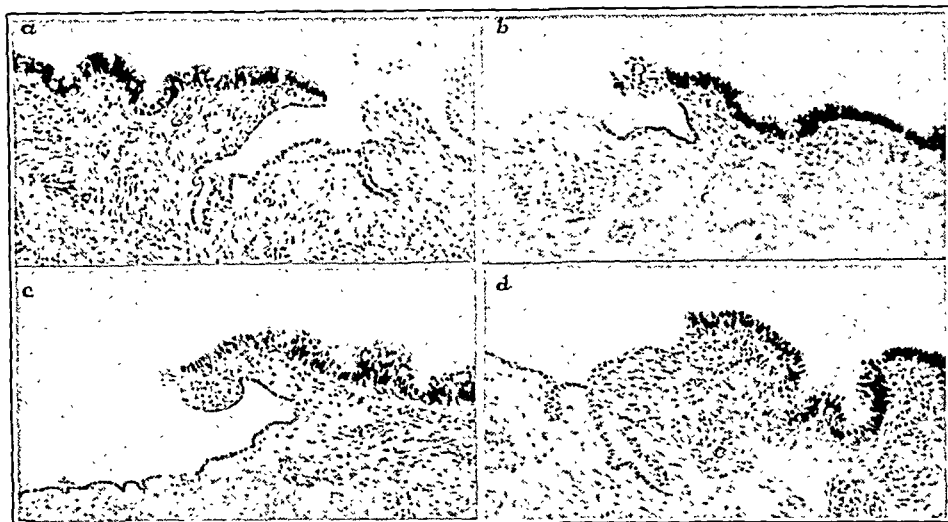


Fig. 3.—Four photomicrographs ( $\times 90$ ) showing the “normal” termination of the epithelium of the fimbrial mucosa at its junction with the mesothelium of the serosa from four different patients. This occurs abruptly, often with a gap between the epithelial covering of the fimbriae and the mesothelial covering of the tube. It constitutes a vulnerable and unstable area apparently easily traumatized and therefore frequently undergoing repair. Photomicrograph “a” shows a common type of mucoserosal union with a very slight break between the tubal epithelium and serosal mesothelium. In “b” there exists at the mucoserosal junction a definite gap through which granulation tissue is protruding and both epithelial and mesothelial cells are being extruded. In “c” an extensive gap, without epithelial or mesothelial covering, is present and possibly represents a partially healed stage of the condition shown in Fig. 2. In “d” a little different type of mucoserosal junction is shown with a definite break between the epithelium and mesothelium, representing possibly an attempted repair of an injury. Operative trauma of the tubal mucosa in tubal stumps is frequently followed by an activation and differentiation of this mucosa causing “endometriosis.” Primary fimbrial endometriosis apparently occurs most frequently in the terminal portion of the tubal mucosa at the mucoserosal junction where trauma and repair often take place.

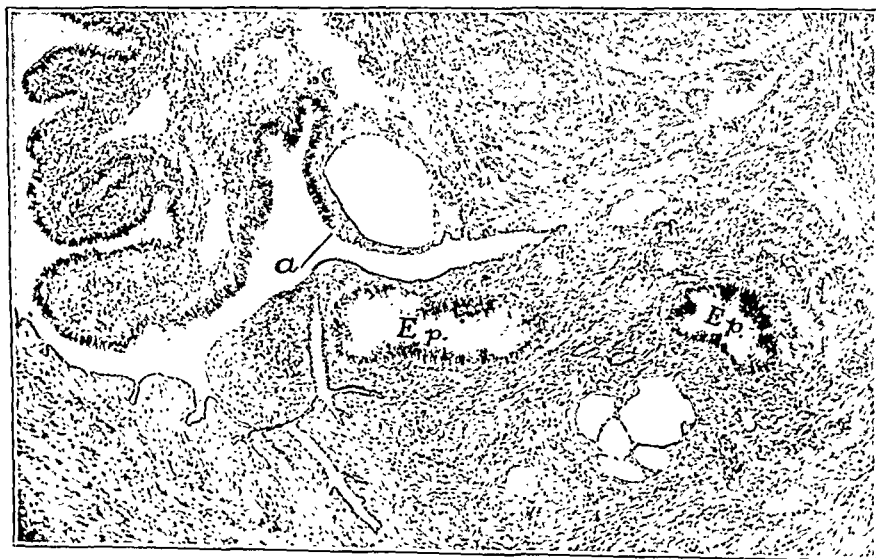


Fig. 4.—Photomicrograph ( $\times 60$ ) is of the mucoserosal junction of an apparently normal tube. The mucosa at the base of the fimbriae ends abruptly at “a” with a slight break between the epithelium and mesothelium. Epithelial inclusions “Ep” are present, thus suggesting a repair of a former injury, but there is no evidence of a differentiation into mucosa of uterine type.



My interest in the fimbriated end of the tube during the last ten years, has resulted in my encountering endometriosis on the serosa of the distal end of the tube in several instances. This was usually of the foreign body type and similar to that frequently found on other pelvic structures including portions of the intestinal tract. During this time I col-



Fig. 5.—Two photomicrographs ( $\times 130$ ) of the mucoserosal junction of fimbriae of a normal appearing tube. The patient had had a previous attack of pelvic peritonitis of probable tubal origin. The photomicrographs are from opposite sides of the same longitudinal section of the fimbriated end of the tube. Note the cellular infiltration of the tissue beneath the terminal portion of the epithelium of the tubal fimbriae and the hyperplasia of this epithelium, even suggesting that some of the epithelium could easily become detached and escape into the pelvic cavity. These reactions were found only in this situation. It suggests that this portion of the tubal fimbriae is more vulnerable than the rest of the fimbriae and therefore more likely to become activated and possibly undergo differentiation if given the proper stimulus. The gland-like space in the lower photomicrograph may be either an inclusion of the tubal epithelium or a cross section of a mucosal pocket or depression.

lected fourteen cases of primary fimbrial endometriosis which had developed from a differentiation of the tubal epithelium of the fimbriae.

Had I studied fimbrial endometriosis from the beginning, with my present knowledge of the subject, I would have found many more instances of this condition. In the four weeks prior to the writing of this

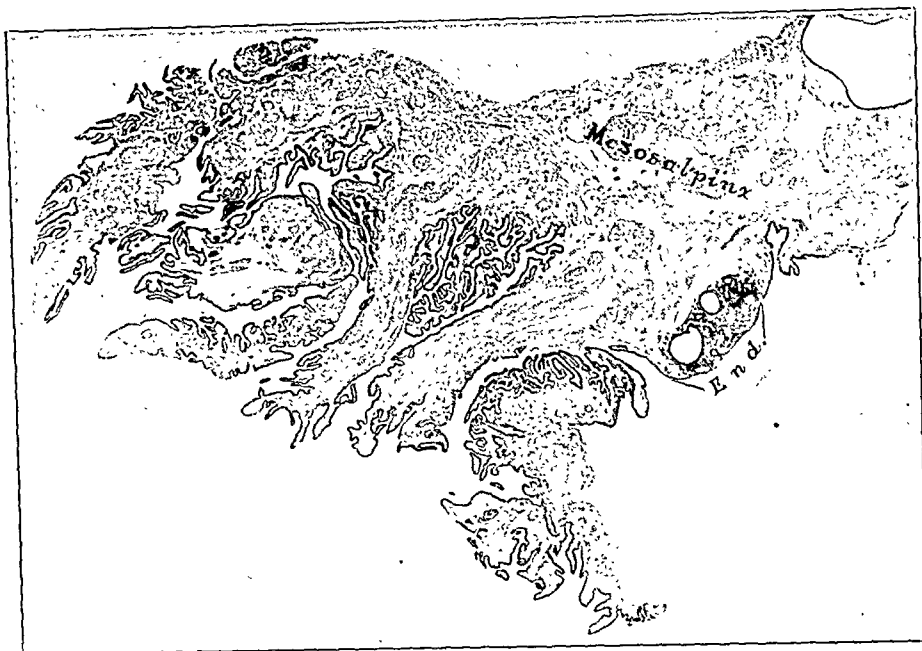


Fig. 6.—Photomicrograph ( $\times 8$ ) of an oblique section of the fimbriae of the right tube and a portion of the mesosalpinx showing a primary fimbrial endometriosis "End." This has developed in tubal mucosa which had spread from the base of the fimbriae over the surface of the mesosalpinx (see Figs. 7 and 36). Note the preponderance of mural fimbriae.

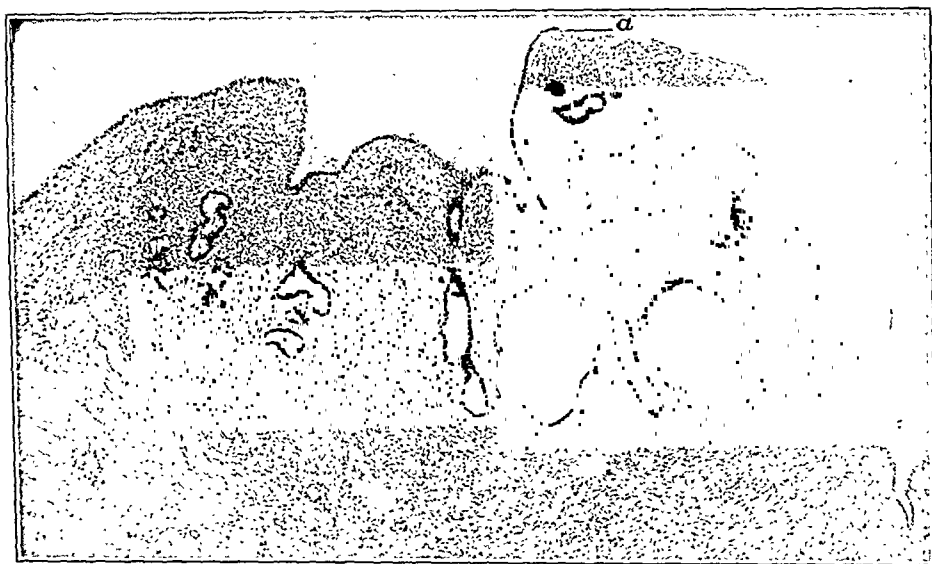


Fig. 7.—Photomicrograph ( $\times 50$ ) of the primary fimbrial endometriosis shown in Fig. 6 but taken at a different level of the same block. The endometriosis has developed in the terminal portion of the tubal mucosa near the mucoserosal junction. The patch of differentiated müllerian mucosa is covered by tubal epithelium up to the place indicated by "a": beyond this point, it is covered by mesothelium. The activated tubal epithelium has invaded the underlying tissues of the mesosalpinx forming glands. The tissue about these glands resembles endometrial stroma into which hemorrhage has occurred, thus suggesting a menstrual reaction. At no place was there any evidence of the origin of glands from the mesothelium.

paper I encountered four instances of primary fimbrial endometriosis the data from which have not been completely studied and are therefore not included in this series.

The following cases have been selected which, with the illustrations and their accompanying legends, should portray the conditions I wish to present.

CASE 1.—Primary fimbrial endometriosis of the right tube associated with endometriosis of the lateral surface of the right ovary, and the peritoneum of the posterior culdesac. The patient, aged thirty-seven, was operated upon January 17, 1922, for a large uterine myoma. On account of irregular uterine bleeding, the exact date of the last menstrual period could not be determined. The appendix, both tubes and



Fig. 8.—Photomicrograph (x8) of a longitudinal section of the fimbriated end of the tube lateral to its lumen, and a portion of the mesosalpinx (Case 2, see Fig. 37). Primary fimbrial endometriosis "End." has developed between two mural fimbriae, "a" and "b." Secondary fimbrial endometriosis "Imp." is present on the serosa of the dorsal surface of mural fimbria "b" near its base (see Fig. 9). A cross section of what might be a rudimentary tubal ostium "Rud. ost." appears at the right (see also Fig. 37) with implantation-like endometriosis on its serosal surface (torn and misplaced in restraining the section).

ovaries and uterus were removed. Both tubes were apparently patent. The fimbrial endometriosis arose from the activation of tubal epithelium at the mucoserosal junction of tubal mucosa which had spread over the surface of the mesosalpinx from the base of the fimbriae (see Figs. 6, 7, and 36).

CASE 2.—Primary fimbrial endometriosis of the right tube associated with a large hemorrhagic cyst of that ovary and endometriosis of the lateral surface of the left ovary, and the peritoneum of the posterior culdesac. The patient, aged thirty-eight, was operated upon November 22, 1923, for a large hemorrhagic cyst of the right ovary (about fifteen centimeters in its greatest diameter). The appendix, both tubes and ovaries and uterus were removed. Both tubes were apparently patent. The fimbrial endometriosis arose from a differentiation of the tubal mucosa just proximal to its mucoserosal junction (see Figs. 8, 9, and 37).

CASE 3.—Primary fimbrial endometriosis of the left tube associated with endometriosis of the lateral surface of the left ovary and the peritoneum of the posterior culdesac. The patient, aged forty-six, was operated upon February 19, 1928, for a large uterine myoma. She expected to menstruate within a day or two of the operation, but began to flow that morning. The appendix, left tube and ovary and uterus were removed. Both tubes were apparently patent. The fimbrial endometriosis arose from a differentiation of the tubal mucosa at or near the mucoserosal junction and by direct extension had invaded the wall of the tube, giving rise to an "endometrial" cavity, the mucosal lining of which showed a characteristic menstrual reaction with evidence that its contents might readily escape into the peritoneal cavity (see Figs. 10, 11, 12 and 38).

CASE 4.—Multiple primary fimbrial endometrioses of the right tube with invasion of the tubal wall but without ovarian or peritoneal endometriosis. The patient, aged

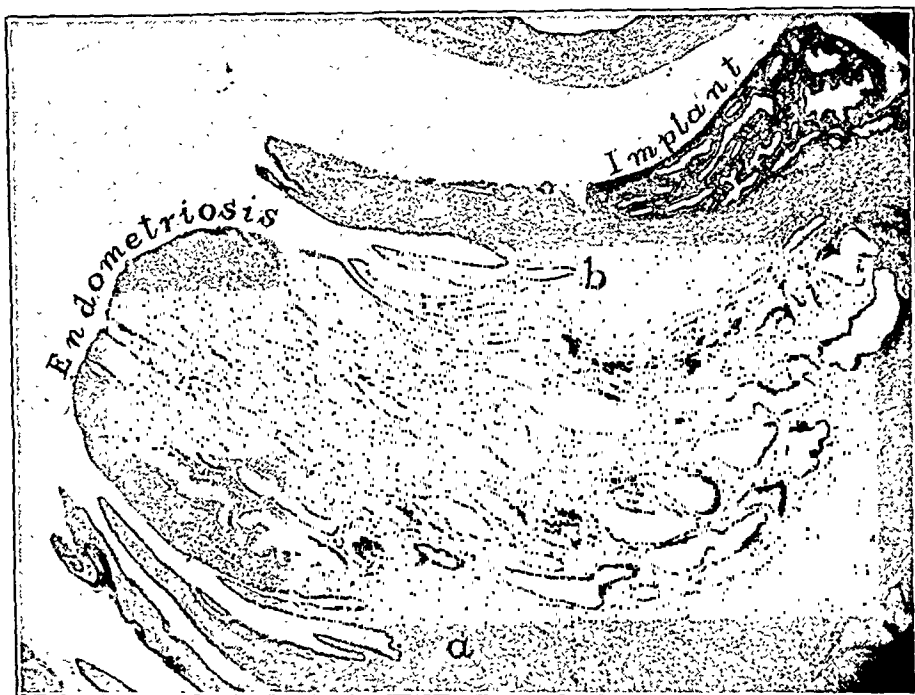


Fig. 9.—Photomicrograph (x25) showing better the origin of the primary fimbrial endometriosis "End." and the situation of the secondary endometriosis "Imp." of Fig. 8. The surface epithelium of the primary endometriosis is continuous with that of the normal fimbriae. The epithelium forming the glands is continuous with the surface epithelium. The endometriosis evidently arose from an activation and differentiation of this epithelium and the tissues invaded by it. The palmar surface of mural fimbriae "b" is covered by epithelium but its dorsal surface by mesothelium, the transition between the two occurring at the tip of the fimbria. The secondary endometriosis on the serosa of the base of this fimbria is of an implantation type, without an epithelial covering and encapsulated, compare with the primary endometriosis above it. The stroma surrounding the glands of this endometriosis resembles that of the endometrium.

forty-three, was operated upon September 23, 1931, twelve hours after the onset of her menstrual period, for the result of the injuries of childbirth and myofibrosis uteri. The uterus, right tube and ovary were removed and the pelvic floor repaired. Both tubes were apparently patent. Multiple hemorrhagic fimbriae of the right tube were present which arose from a differentiation of the tubal mucosa apparently at or near their mucoserosal junction. Endometriosis was present in the wall of the tube and apparently arose from the direct extension of the fimbrial endometriosis (see Figs. 13, 14, 15, and 39).



Fig. 10.—Two photomicrographs (x8) of cross sections of the distal end of the tube at the base of the fimbriae showing primary fimbrial endometriosis with invasion of the mesosalpinx by this tissue (Case 3, see also Fig. 38). The first shows the relation of the differentiated fimbriae, "End." to the normal fimbriae below it. From its situation it must have arisen in the terminal portion of the fimbrial mucosa although the mucoserosal junction was not definitely determined. The second demonstrates the origin of an endometrial cavity, "End. Cav.," in the mesosalpinx from the invasion of this structure by the differentiated tissue of the fimbrial endometriosis. The section is incomplete and shows only the base of the differentiated fimbria "End." The patient began to menstruate the morning of the operation. Blood was present in the stroma of the fimbria and also in the endometrial cavity (see Fig. 11). It is conceivable that müllerian tissue with menstrual blood might escape into the pelvis through a potential perforation, at "p," and become implanted on the peritoneum, as such tissue becomes implanted when it is disseminated from similar cavities (cysts) of the ovary.



Fig. 11.—Photomicrograph (x60) of a portion of the wall and mucosal lining of the endometrial cavity shown in the preceding section. A characteristic reaction to menstruation is present, the lumen of the cavity containing blood and cast-off epithelium which might escape through the potential perforation of the wall of this cavity indicated by "p" of Fig. 10.

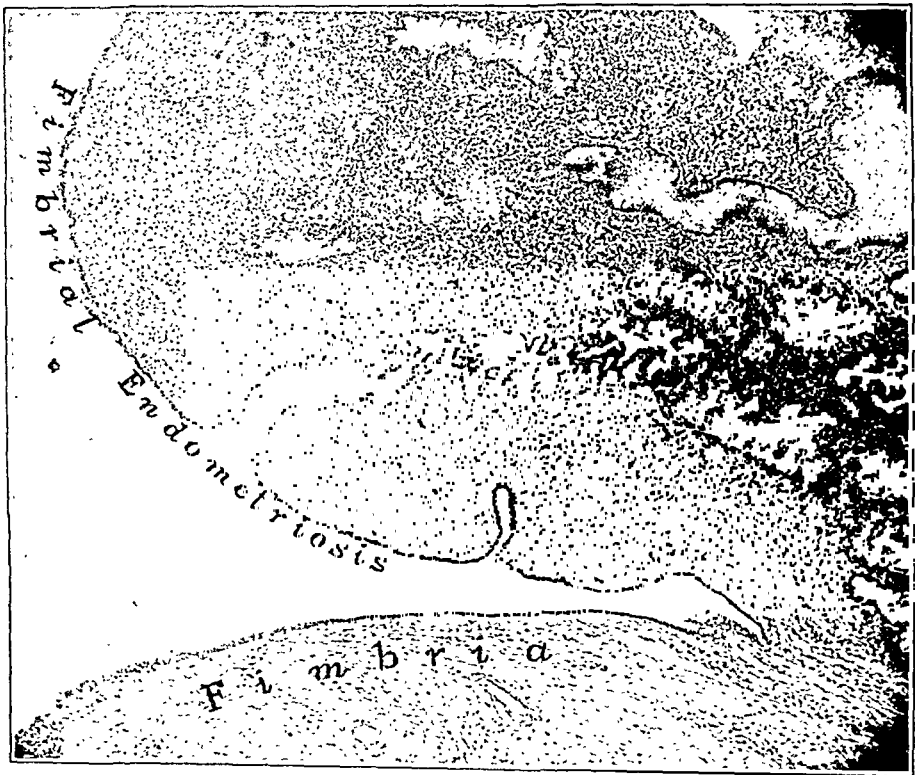


Fig. 12.—Photomicrograph (x60) of a portion of the differentiated fimbria "End." of the upper photomicrograph of Fig. 10. The epithelial covering of the fimbrial endometriosis is continuous with that of the normal fimbria below it. The glands arose from surface epithelium of tubal type; other portions of this fimbria were covered by epithelium of an indefinite type. The mucoserosal junction was not determined.

CASE 5.—Primary fimbrial endometriosis of the left tube, causing a tuboovarian endometrial cyst, associated with peritoneal endometriosis in the posterior culdesac and an intracervical carcinoma. The patient, aged thirty-seven, was operated upon November 9, 1931. The preoperative diagnosis was extensive peritoneal endometriosis. The last menstrual date was not determined on account of irregular uterine bleeding. On exposing the pelvic contents, the right tube and ovary appeared normal. The left ovary was enlarged and adherent by its lateral surface to the posterior layer of the left broad ligament and to the side of the pelvis. On freeing the ovary, old



Fig. 13.—Photomicrograph ( $\times 7$ ) of a longitudinal section of the fimbriated end of a tube through the center of its lumen (Case 4, see also Fig. 39). Two mural fimbriae "a" and "b" appear in oblique section, each the seat of a primary endometriosis. Endometriosis is also present in the wall of the tube. For the relation between the endometriosis of the fimbriae and that of the tubal wall (see Fig. 14) and for the origin of the fimbrial endometriosis (see Fig. 15).

blood escaped, and it was noted that the fimbriated end of the patent tube protruded into the cavity of an ovarian cyst. The wall of the cyst was torn at this place, but fortunately a portion of the attachment of the tube to the cyst was not disturbed (Fig. 16).

The lower portion of the posterior culdesac was obliterated by an extensive endometriosis. The appendix, both tubes, ovaries and entire uterus were removed. The bottom of the culdesac was curetted and a large amount of müllerian mucosa was removed (see Fig. 19). On incising the uterus, after its removal, an unsuspected



Fig. 14.—Photomicrograph ( $\times 7$ ) of a longitudinal section of the fimbriated end of the tube shown in Fig. 13, from the same block, but near the periphery of the tube. Serial sections were not made and therefore the relation between the endometriosis of the fimbriae shown in this and in Fig. 13 was not determined. The endometriosis of the tubal wall is the same as that shown in Fig. 13. Note the proximity of the endometriosis of the tubal wall, "End.," to that of the base of fimbria "b" suggesting that the endometriosis of the tubal wall arose, by direct extension, from the fimbrial endometriosis as in Fig. 10. I was unable to definitely establish this connection. If present it was lost in trimming the block. The section shown in this illustration was the first complete section from the block.



Fig. 15.—Photomicrograph ( $\times 25$ ) of a portion of mural fimbria "a" shown in Fig. 13. The dorsal (upper) surface of the fimbria is covered by mesothelium except at the extreme right where both mesothelium and epithelium are lacking. The palmar surface (below) is covered by tubal epithelium, patchy towards the right. The tubule or gland "g" has arisen from a patch of tubal epithelium on the surface of the fimbria and from its situation must represent the terminal portion of the fimbrial mucosa at or near the mucoserosal junction. The endometriosis of the fimbria evidently arose from the activation and differentiation of the tubal epithelium covering it. There is an extravasation of blood in the stroma of the fimbria, probably due to a menstrual reaction. The operation occurred twelve hours after the onset of menstruation.



early intracervical carcinoma was found. Sections were made through the fimbriated end of the tube and the wall of the ovarian cyst (Fig. 16). The müllerian mucosa lining the cyst was continuous with that of the tubal fimbriae (see Figs. 17 and 18).

CASE 6.—Primary fimbrial endometriosis of the left tube, causing a tuboovarian endometrial cyst associated with endometriosis of the mucosa of the left tube, an endometrial cyst of the opposite ovary, extensive peritoneal endometriosis especially in the posterior culdesac with extension through to the posterior vaginal vault, and myoma uteri. The patient, aged twenty-nine, was operated upon November 27, 1926, two weeks after her last menstrual period, for bilateral ovarian hematomas. On exposing the pelvic contents, at operation, the pelvic structures were found to be covered with old blood. The endometrial cyst of the right ovary was about 10 cm. in diameter, the tube appeared normal. The endometrial cyst of the left ovary was

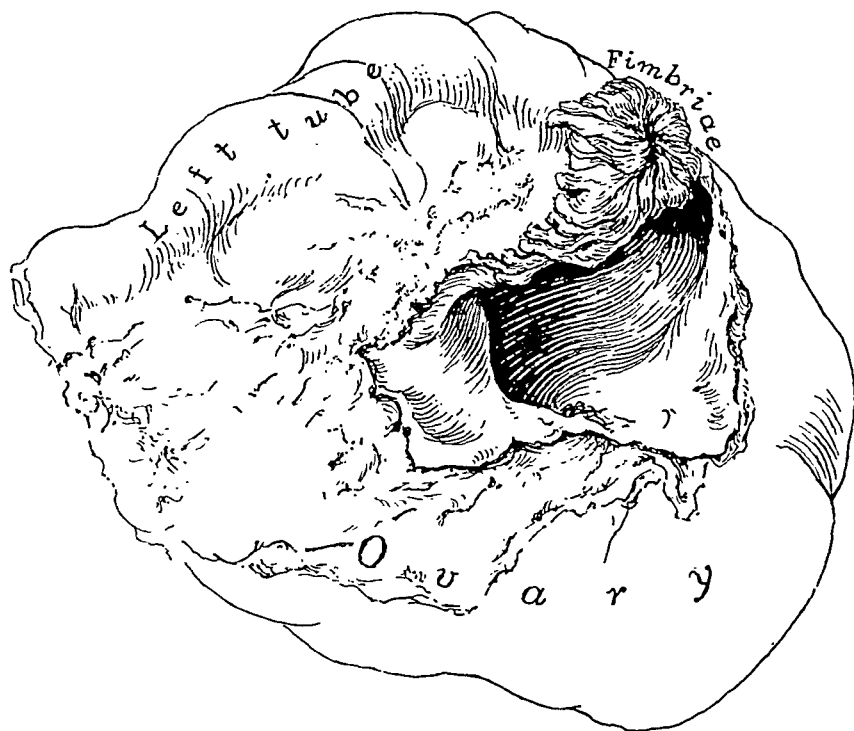


Fig. 16.—A sketch of the anterior or lateral view of the left tube and ovary (Case 5). The fimbriated end of the tube opened into the cavity of the cyst thus forming a tuboovarian cyst. This relation was partially disturbed in freeing the adherent ovary at the operation. For the origin of the lining of the endometrial cyst from the differentiated mucosa of the tubal fimbria (see Figs. 17 and 18).

about 6 cm. in diameter. The left tube was patent and opened into the cavity of an endometrial cyst of that ovary, thus forming a tuboovarian cyst. The appendix, uterus and both tubes and ovaries were removed. For further description of the condition found see Figs. 20, 21, 22, 23, and 24.

CASE 7.—Primary fimbrial endometriosis of the left tube associated with endometriosis of the lateral surface of the left ovary, the posterior layer of the left broad ligament and peritoneum of the posterior culdesac. The patient, aged forty-one, was operated upon June 7, 1930, the third day of her menstrual period, usually of seven to eight days' duration, for a large myomatous uterus. On exposing the pelvic contents a small amount of blood was present in the pelvis. The left ovary was fused by its lateral surface with the posterior layer of the left broad ligament. The appendix, left tube and ovary and uterus were removed. Both tubes were apparently

patent. The portion of the posterior layer of the left broad ligament, adherent to the lateral surface of the ovary, was carefully removed with the ovary. The tube, ovary and portion of peritoneum attached to the latter were fixed in formalin and sections were made in a horizontal plane. An endometrial cavity (cyst) had developed between the lateral surface of the left ovary and the portion of the posterior layer of the broad ligament adherent to the ovary. Patches of endometriosis were found on the lateral surface of the ovary and on the surface of the mesosalpinx, ex-



Fig. 17.—Two photomicrographs (x7) of longitudinal sections, at different levels, of the fimbriated end of the tube and a portion of the wall of the ovarian cyst into the cavity of which the fimbriated end of the tube opened (see Fig. 16). At "a" of the upper photomicrograph, the differentiation of the terminal portion of the mucosa of the fimbria (probably an ovarian fimbria) into mucosa of endometrial type is well shown (see Fig. 18). By serial sections it was shown that the differentiated mucosa indicated by "b," a continuation of "a," is also continuous with that of "c" of the lower photomicrograph which in turn is continuous with the mucosal lining of the endometrial cyst of the ovary, a portion of the wall of which is fused with the wall of the tube. Therefore the endometrial cyst of the ovary arose from the activated and differentiated mucosa of the tubal fimbria as similar cysts may arise from the activated and differentiated mucosa of a tubal stump (see Fig. 1).

tending up to the base of the ovarian fimbria where the primary endometriosis had arisen from a differentiation of the terminal portion of the tubal mucosa at the mucoserosal junction. A similar differentiation of fimbrial epithelium was present at the base of fimbriae on the opposite side of the tube. This had invaded the mesosalpinx. For a further description of the condition found see Figs. 25, 26, 27, and 28.

CASE 8.—Probable primary fimbrial endometriosis of the right tube associated with an endometrial cyst of the right ovary and peritoneal endometriosis. The patient, aged thirty, was operated upon November 8, 1922, in the interval stage of her menstrual cycle, for an adherent, retroflexed myomatous uterus. On exposing the pelvic contents, old blood was present in the culdesac coming from a partially collapsed endometrial cyst of the right ovary, about three centimeters in its greatest diameter. The appendix, right tube and ovary and uterus were removed. Both tubes were apparently patent. Endometriosis had developed at the mucoserosal junction of the ovarian fimbriae (see Figs. 29 and 40).



Fig. 18.—Photomicrograph (x60) of the terminal portion of the mucosa of the tubal fimbria shown at "a" of the upper photomicrograph of Fig. 17. The normal tubal fimbriae appear at the left. One can see the gradual transformation of their normal tubal mucosa into mucosa of uterine type: similar to the transition of the epithelium of normal mucosa to cancer. The mesothelium apparently has not taken an active part in the origin of this differentiated mucosa but is being overridden and destroyed by it as by the advancing margin of a new growth.

CASE 9.—Endometriosis of the left tube, of probable implantation origin, associated with extensive endometriosis of the right uterine cornu, endometrial implants on the anterior surface of the uterus about the origin of both round ligaments and on the under surface of the left ovary. The patient, aged thirty-eight, was operated upon January 12, 1925, during the interval stage of her menstrual cycle, for the results of the injuries of childbirth and dysmenorrhea. The appendix, left tube and ovary and uterus were removed, and the pelvic floor repaired. Both tubes were apparently patent. I was unable to determine the origin of the endometriosis of the right uterine cornu, whether from the mucosa of the intramural portion of the tube or from implantations on the peritoneal surface of the cornu. For a comparative study of the endometriosis of the tubal fimbria, the peritoneum of the left uterine cornu and the ovary, see Figs. 30 and 31.

CASE 10.—Multiple small nodules of granulation tissue on the fimbriae of the right tube associated with endometriosis of the lateral surface of the right ovary, posterior surface of the uterus, the peritoneum of the posterior culdesac and the cecum. The patient, aged thirty-one, was operated upon September 26, 1922, the second day of her menstrual period, for an adherent retroflexed uterus. On exposing the pelvic contents, blood was observed escaping through the abdominal ostium of both tubes. The uterus, right tube and ovary and appendix were removed. For the description of the fimbrial lesions of the right tube, see Figs. 33 and 41.

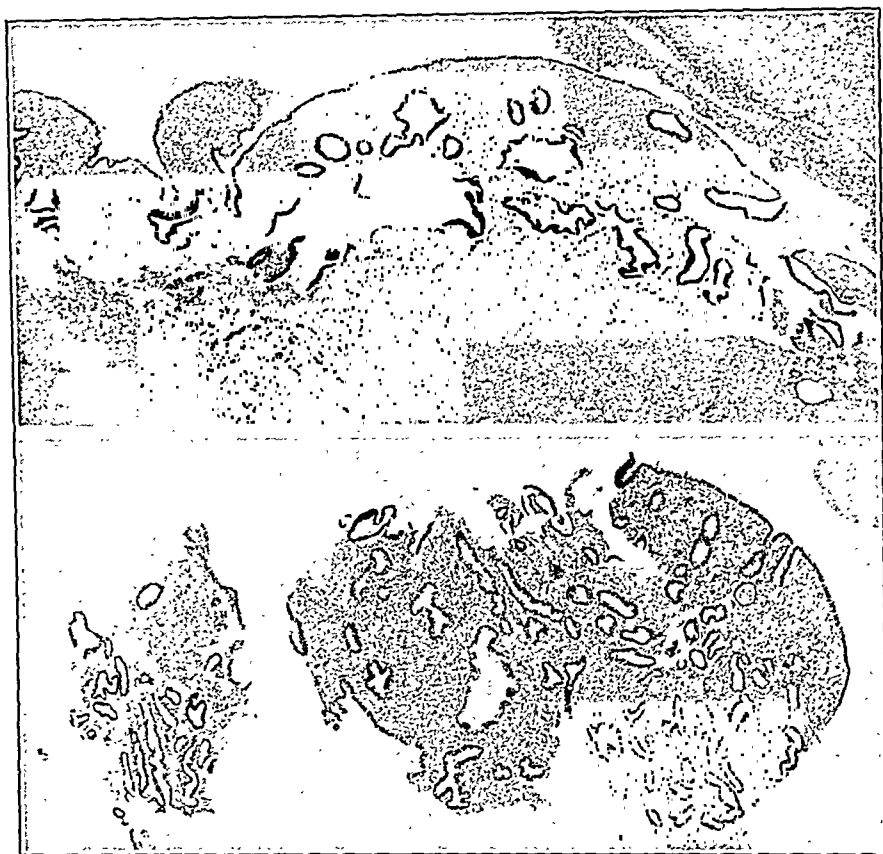


Fig. 19.—Two photomicrographs (x25), the upper one is of the endometrial lining of the ovarian cyst shown in Fig. 17, and the lower is of tissue curetted from the bottom of the posterior culdesac of the same case. The histologic structure of the mucosa in the two sections is the same. We have demonstrated the origin of the müllerian lining of the cyst. How shall we account for that in the culdesac?

CASE 11.—Endometriosis of the serosa of the left tube near the mucoserosal junction of the fimbriae associated with endometriosis in the posterior culdesac. The patient, aged twenty-six, was operated upon November 28, 1928, for conditions resulting from the injuries of childbirth and for uterine bleeding. A curettage of the uterus, amputation of the cervix and repair of the pelvic floor was done first. This was followed by an abdominal section. On exposing the pelvic contents a small amount of blood was found in the posterior culdesac, the left tube was slightly distended with blood which was oozing through its abdominal ostium. The appendix, left tube and ovary were removed and a tubal sterilization on the right side and ventral fixation of the uterus was done. Endometriosis was detected only on serosa of the distal end of the left tube (see Figs. 34 and 35) and in the posterior culdesac. The microscopic examination of sections of the left tube showed the remains of an early tubal pregnancy.

A study of the conditions in the cases just reported (see also the illustrations and their legends), as well as material from other similar cases demonstrates that endometriosis may arise from a differentiation of the mucosa of tubal fimbriae into a structure resembling endometrium. This differentiated and activated mucosa may invade or spread over the surfaces of the wall of the tube and the mesosalpinx. When it arises

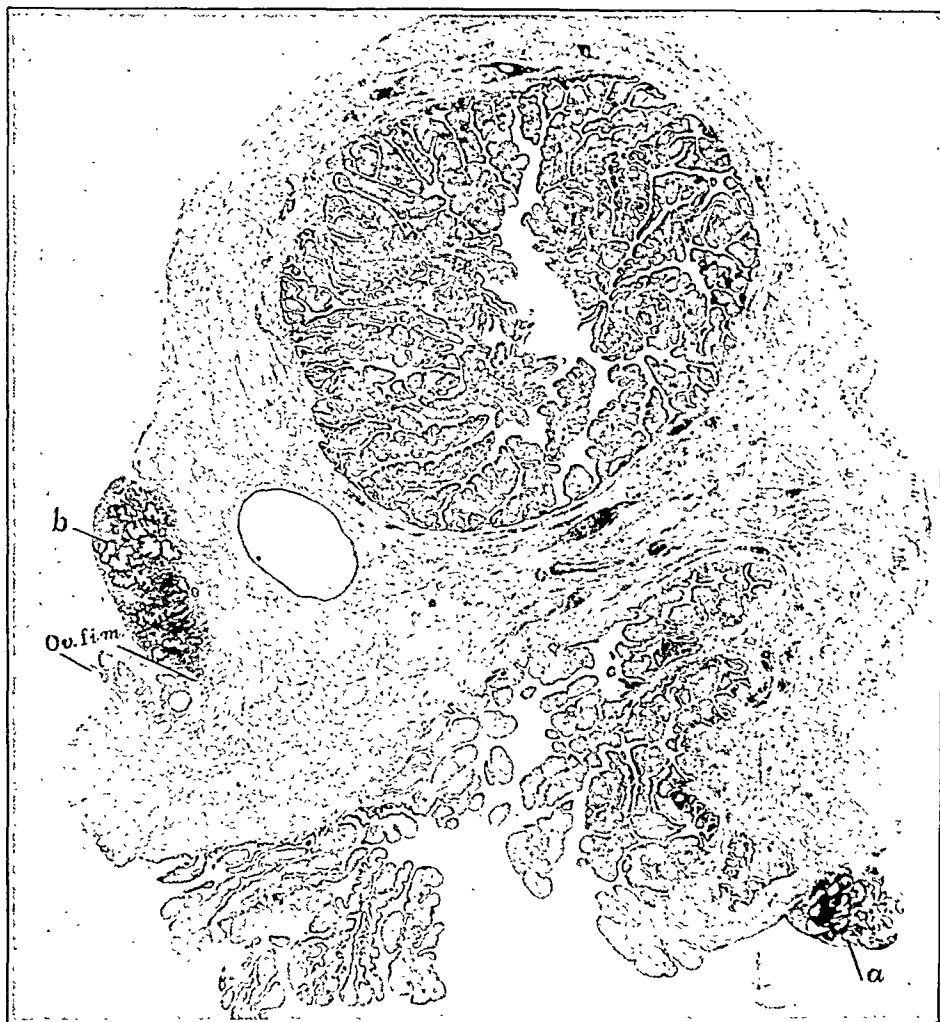


Fig. 20.—Photomicrograph ( $\times 7$ ) of a slightly oblique section of the fimbriated end of the tube (Case 6). The ampulla of the tube appears above in cross section. The fimbriated end of the tube opened into the cavity of an endometrial cyst of the ovary as in Fig. 16 of the preceding case. Two patches of fimbrial endometriosis are present, both arising from an activation and differentiation of the terminal portion of the tubal mucosa at the base of fimbriae. For a higher magnification of endometriosis "a" (see Fig. 21). Endometriosis "b" is situated at the base of an ovarian fimbria "Ov. fim." The continuity between the main tubal fimbriae and the ovarian fimbriae is evident in preceding sections from the same block.

in ovarian fimbriae it may likewise involve the ovary sometimes causing endometrial cysts of that organ.

In three of the cases, with an associated ovarian endometrial cyst, the endometrial lining of the cyst was demonstrated to be continuous with the endometriosis arising from the fimbrial mucosa. Two of these are reported in this paper (see Figs. 17 and 22).

In three patients operated upon during their menstrual period a typical menstrual reaction was present in the fimbrial endometriosis (Figs. 10, 13, and 27) and in two of these a similar reaction occurred in the endometriosis associated with and derived from the fimbrial endometriosis (Figs. 11 and 27). Bits of müllerian tissue must escape into the peritoneal cavity from this menstruating mucosa and should have the same potentialities of implantation as those escaping from similar lesions in the ovary.

Primary fimbrial endometriosis, in the cases in which I have been able to determine the exact site of its origin, has developed in the terminal



Fig. 21.—Photomicrograph ( $\times 25$ ) of fimbrial endometriosis "a" of Fig. 20, showing its origin from the tubal mucosa at the mucoserosal junction. The differentiated mucosa has spread (ridged) over the serosa of the tube as indicated by inclusions of the mesothelium "m" beneath it. The distal portion (to the left) of this patch of endometriosis was evidently torn during the operation.

portion of the tubal mucosa of the fimbriae at or near the mucoserosal junction. I believe that it may arise in other portions of the fimbriae because I have encountered two instances, in this series, in which endometriosis had arisen in the mucosa of the ampulla of the tube. One of these is described in this paper in Figs. 22 and 24.

This series of only fourteen cases of primary fimbrial endometriosis is too small in number to be of any statistical value. Nevertheless it suggests that the conditions present in the terminal portion of the mucosa of the fimbriae constitute an important factor in the etiology of the differentiation of tubal mucosa into mucosa of uterine type. It is well known that endosalpingiosis of nonoperative origin occurs most frequently in the intramural portion of the tube where the transition usually takes place from uterine to tubal epithelium, apparently a vulnerable area. There is present at the mucoserosal junction of the fimbriae also a transition from one type of cellular covering to another.

The repair of operative trauma of the mucosa of the tube in tubal

stumps is frequently followed by an activation of this mucosa which may invade not only the stump but also any organ or structure normally continuous with the stump or becoming adherent to it. The misplaced tubal mucosa arising from the outgrowth of the traumatized mucosa of the stump may become differentiated into mucosa of the structure and function of the endometrium (see Fig. 1). I have demonstrated, in the present study, that the extension of the differentiated mucosa of primary fimbrial endometriosis causes endometriosis in adjacent structures, in-

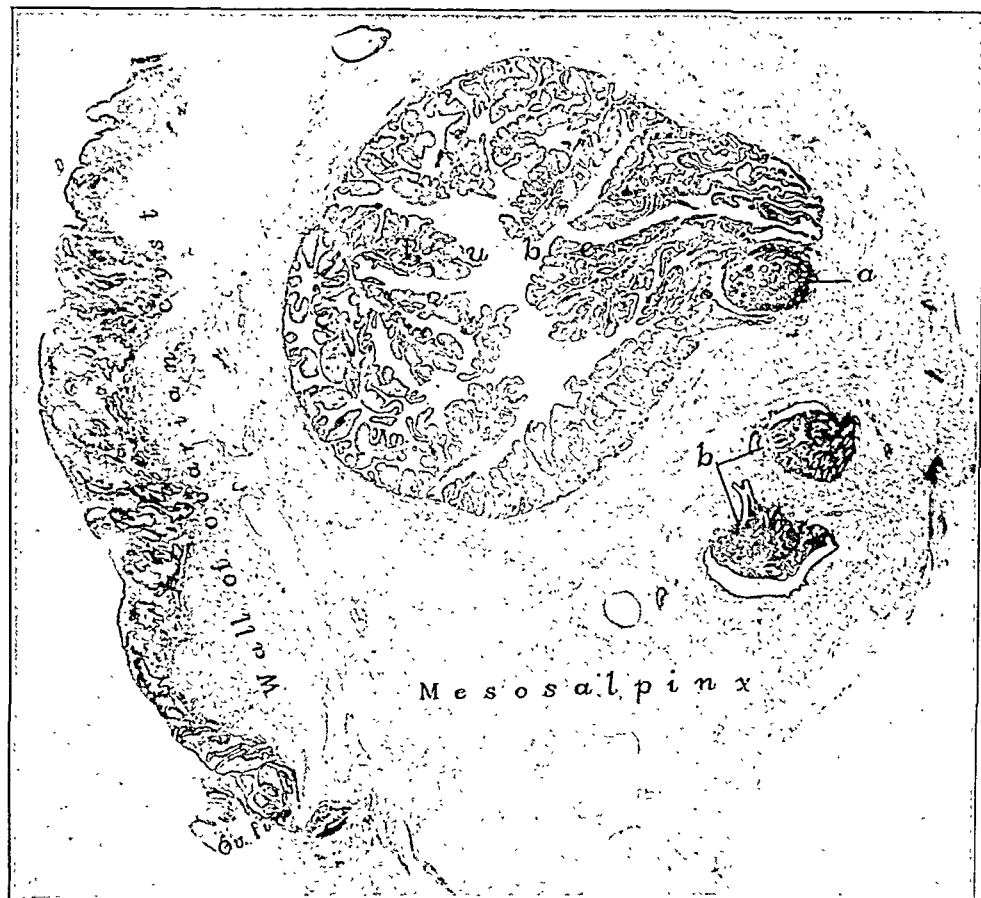


Fig. 22.—Photomicrograph (x7) of a cross section of the ampulla of the tube and a portion of the adherent wall of the endometrial cyst of the ovary into the cavity of which the fimbriated end of the tube emptied. This section is proximal to that of Fig. 20. Ovarian fimbriae "Ov. fim." still appear at this level. The endometrium-like lining of the cyst is continuous with the differentiated mucosa arising in the terminal portion of the tubal mucosa at the mucoserosal junction of the fimbriae as in Fig. 17 of the preceding case. Endometriosis "a" is present in the mucosa of the ampulla of the tube, for its origin see Fig. 24. I was unable to determine the source of the endometriosis "b" in the wall of the tube, whether from the endometriosis of the tubal mucosa above it or from an implant on the surface of the tube lateral to it.

cluding endometrial cysts of the ovary, similar to those following the repair of tubal stumps. Can a like etiology for the two conditions be demonstrated? The abrupt ending of the tubal mucosa at the mucoserosal junction of the fimbriae often with a gap between the epithelium and mesothelium, may simulate the severed mucosa of a tubal stump. The frequent evidence of minor injuries in this situation and their re-

pair even in normal appearing tubes, as illustrated in Figs. 3, 4, and 5, are indications of the vulnerability of the tissues at this mucoserosal junction. The general laws governing the repair of injuries of the various organs and structures of the body are the same whether caused by



Fig. 23.—Photomicrograph (x60) demonstrating the development (origin) of the lining of the endometrial cyst of the ovary (see Fig. 22) from the mucosa of the fimbriae. The transition (differentiation) of the mucosa of the fimbriae (to the left) into the endometrium-like mucosa of the cyst is well shown.



Fig. 24.—Photomicrograph (x25) demonstrating the differentiation of the mucosa of the ampulla of the tube into endometrium-like mucosa. It was shown, by serial sections, that endometriosis "a" of Fig. 22 was continuous with this.



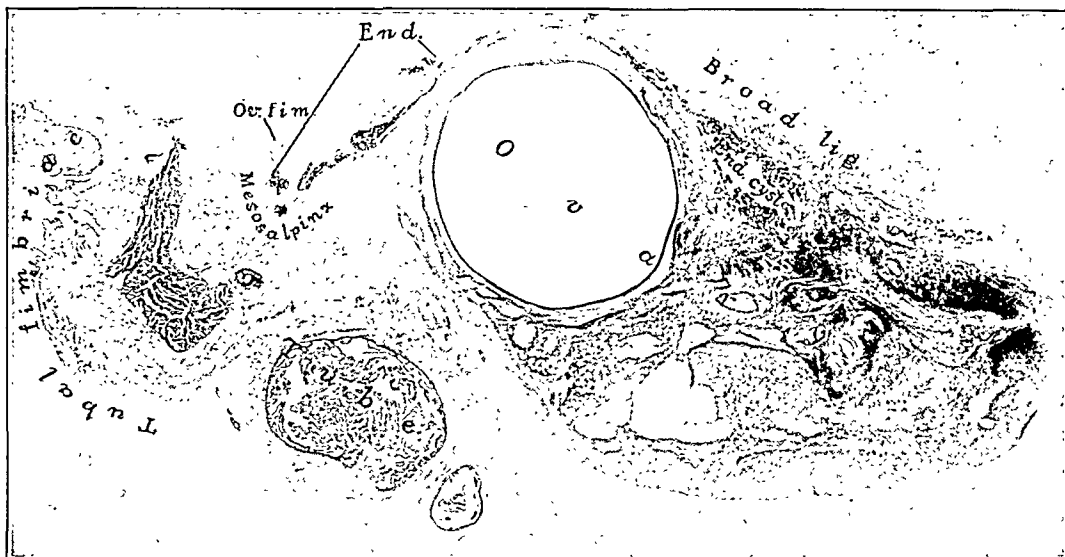


Fig. 25.—Photomicrograph ( $\times 3\frac{1}{2}$ ) of a horizontal section of the distal third of the left tube and mesosalpinx, the entire ovary and the part of the posterior layer of the broad ligament adherent to the ovary (Case 7). An endometrial cavity (cyst) "End. cyst" is situated between the lateral surface of the ovary and the adherent broad ligament. The ovarian fimbriae "Ov. fim.," torn at their origin, extend only a short distance over the free margin of the mesosalpinx. From the base of these fimbriae (see also Fig. 26) endometriosis "End.," appearing in patches, has spread over the surface of the mesosalpinx and extends to and even over the surface of the ovary towards the endometrial cyst.

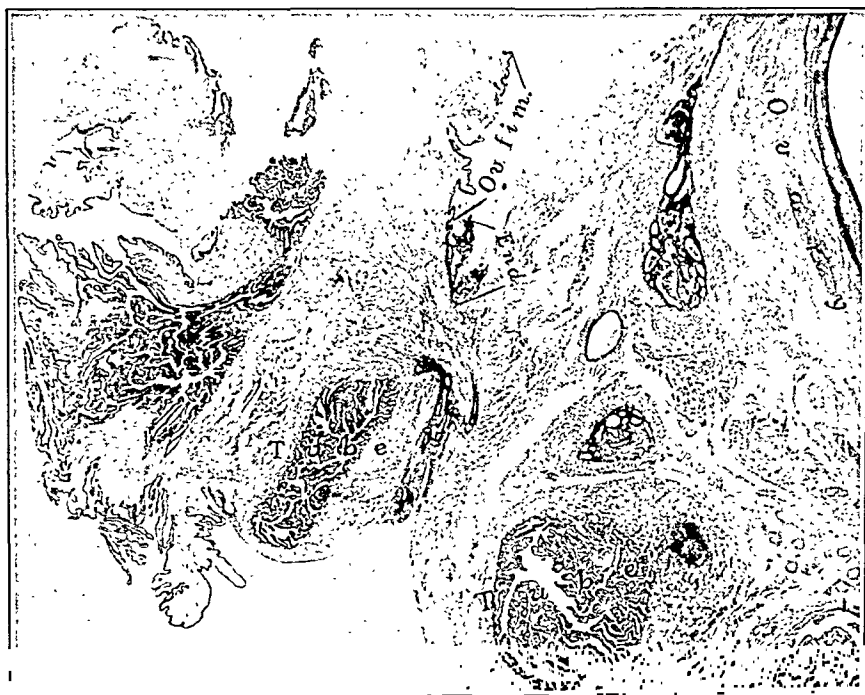


Fig. 26.—Photomicrograph ( $\times 8$ ) of a section of the fimbriated end of the tube and part of the ovary shown in the preceding illustration, from the same block and very near the other. Some of the tubal fimbriae, including the proximal ovarian fimbriae were torn in trimming the block, but fortunately the distal portion of the ovarian fimbriae, "Ov. fim.," is shown in this photomicrograph with endometriosis, "End.," arising at their mucoserosal junction (see Fig. 27). Endometriosis is present on the surface of the tube, the ovary and in the mesosalpinx. For the origin of the endometriosis in these situations see Fig. 28.

Ov. f.



Fig. 27.—Three photomicrographs (the first  $\times 25$  and the others  $\times 60$ ). The first one is of a higher magnification of the patches of endometriosis extending from the base of the ovarian fimbriae, "Ov. fm.," over the surface of the mesosalpinx and ovary shown in Fig. 25. The second is of a higher magnification of the terminal portion of the ovarian fimbria shown in Fig. 26, better demonstrating the development of the fimbrial endometriosis from the tubal mucosa than in the first section which was badly torn at this place. The normal fimbrial mucosa is shown above and the differentiated mucosa below. The third is of a portion of the lining of the ovarian endometrial cyst shown in Fig. 25. The operation occurred on the third day of the patient's menstrual period which usually lasted seven or eight days. The differentiated müllerian mucosa arising from the tubal fimbriae and that lining the ovarian cyst show the same reaction to menstruation with evidence of a loss of müllerian tissue including epithelium. Bits of müllerian tissue escaping from this menstruating tubal mucosa should have the same potentialities of implantation as similar tissue escaping from the ovarian cyst. It is conceivable that the endometriosis arising from the tubal fimbriae is the primary lesion and by direct extension or implantation caused the endometriosis to spread from the fimbriae over the surface of the mesosalpinx and the ovary. If true, the endometrial cyst of the ovary (Fig. 25) probably arose from this source.



Fig. 28.



Fig. 29.

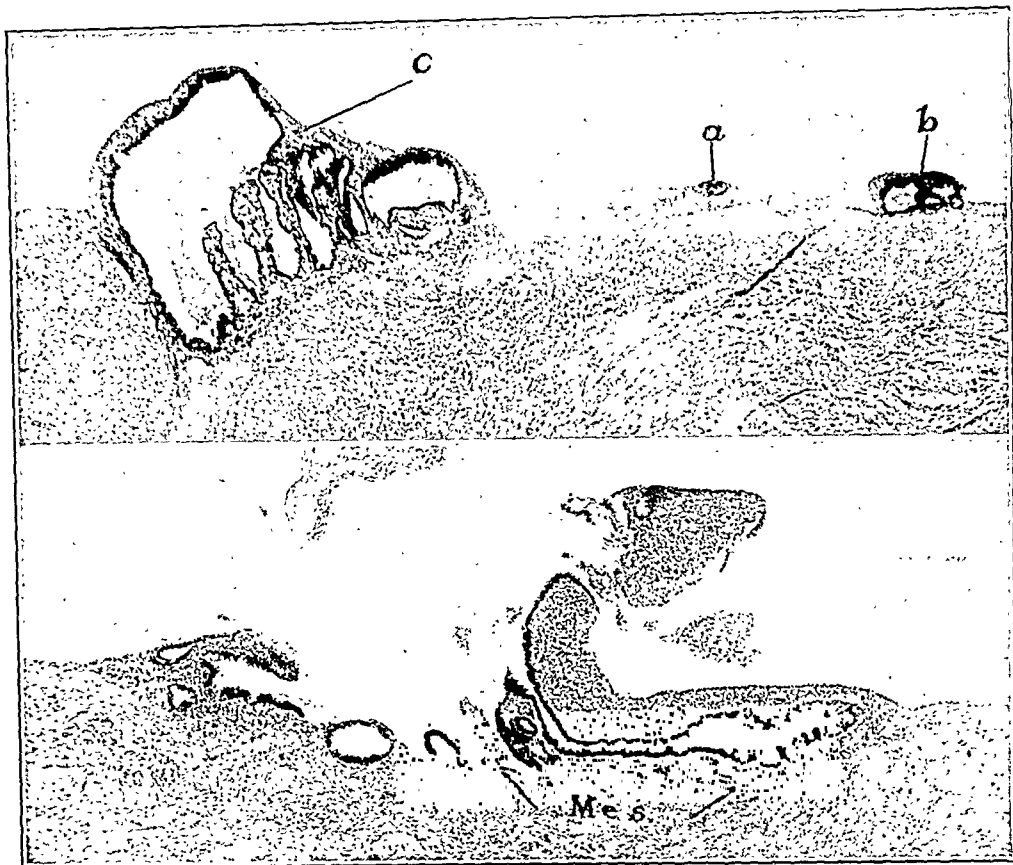


Fig. 30.

Fig. 28.—Photomicrograph ( $\times 8$ ) of a section from the same block as the section shown in Fig. 25, but at a different level. Endometriosis, "End." has developed in the terminal portion of the fimbrial mucosa (see insert). The insert is of a ( $\times 45$ ) magnification of the area "End." of the larger photomicrograph. Normal fimbriae are present at the left. Endometriosis has developed in the terminal portion of their mucosa. A characteristic reaction to menstruation is present in this differentiated mucosa with evidence of blood having escaped into the peritoneal cavity, and a resulting loss of the surface epithelium as in Fig. 27. The fimbrial endometriosis in this section is on the opposite side of the tube from that shown in Fig. 26. A small amount of blood was found in the pelvis at the operation and probably came from these menstruating fimbriae. The endometriosis in the mesosalpinx of Fig. 26 is also shown in the larger photomicrograph of this illustration—see arrows.

Fig. 29.—Photomicrograph ( $\times 8$ ) of a longitudinal section of the fimbriated end of the tube lateral to its lumen (Case 8). Endometriosis "End." is present in the mesosalpinx, evidently having developed at the base of the ovarian fimbriae (see Fig. 40) at or near their mucoserosal junction. I was unable to trace its origin from either tubal epithelium or mesothelium. While I cannot exclude an implantation, circumstantial evidence indicates that it was derived from tubal mucosa.

Fig. 30.—Two photomicrographs illustrating peritoneal endometriosis of probable implantation origin on the surface of the uterus and a tubal fimbria (Case 9). The first ( $\times 10$ ) shows three stages (a, b, and c) in the growth of müllerian implants on the anterior surface of the uterus near the origin of the left round ligament. For a higher magnification of implants "a" and "b" see Fig. 31. The second ( $\times 20$ ) is of endometriosis on the dorsal surface of a peripheral tubal fimbria of the left tube. The endometriosis has developed on the surface of the fimbria covered by peritoneum. Mesothelial inclusions "mes." are situated beneath the right half of the implant. Evidently the capsule of the implant had been torn at the operation. I believe that, before the injury, the structure of this implant was similar to implant "c" shown above and that it had a like origin.

operation or by disease. I believe we can state that since injury and repair of operative trauma of the mucosa of tubal stumps are important factors in the development of endometriosis in this situation, in like manner injury and repair at the mucoserosal junction may be important factors in the development of the fimbrial endometriosis. Since endometriosis does not arise in all tubal stumps or in all or even a large per-



Fig. 31.—Three photomicrographs ( $\times 60$ ). The first is of implant "a" and the second of implant "b" shown in the upper photomicrograph of the preceding illustration. The second implant appears older than the first. The third is of a section through an implant on the lower surface of the left ovary, from the same patient. The histologic structure of the three lesions is the same and therefore suggests a like origin. Their general structure is identical with that resulting from the healing of wounds caused by foreign bodies lodging on the peritoneum with the retention of these bodies in the scar of the wound caused by them (see Fig. 32).

centage of tubal fimbriae we must conclude that additional factors are essential for its development.

Can it be shown that the primary fimbrial endometriosis which usually appears to develop at or near the mucoserosal junction of fimbriae, arises only from tubal epithelium and not from the near-by mesothelium? In nearly all cases of fimbrial endometriosis of this type which I have

studied, the surface epithelium of the differentiated müllerian mucosa was continuous with that of the normal mucosa of the fimbriae and in not a single instance could it be shown that it arose from the mesothelium (Figs. 18, 21 and 23). In two instances in which I was unable to demonstrate the continuity of the surface epithelium in the two conditions this epithelium was lacking at the junction due to a menstrual reaction in one instance and possibly to the trauma of operation in another. Could primary fimbrial endometriosis be of other origin and arise from

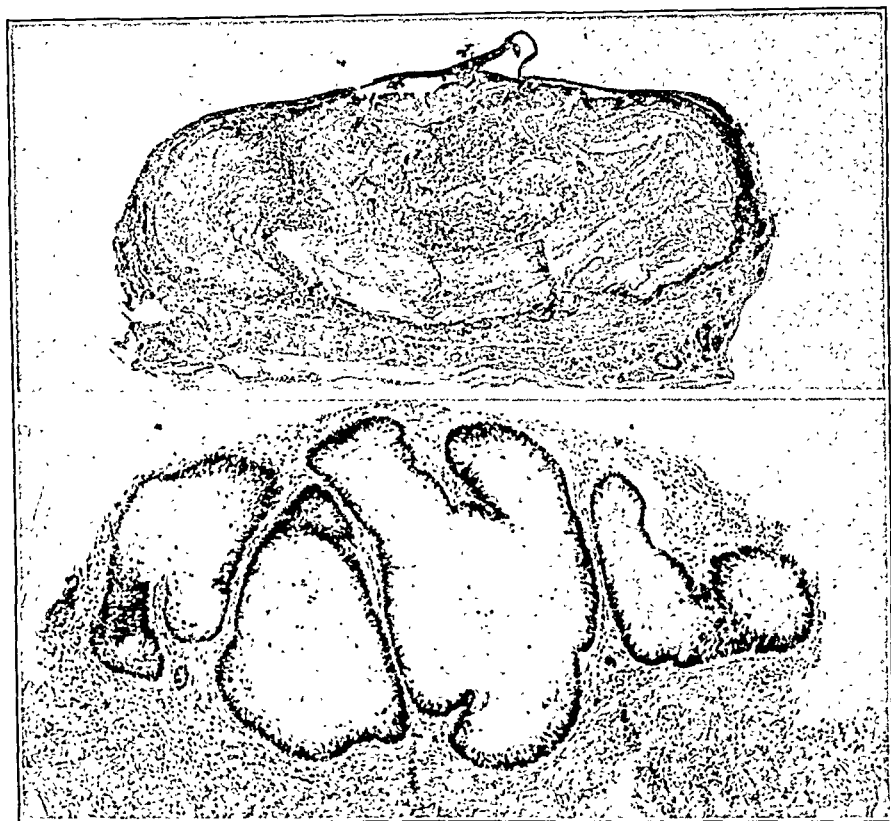


Fig. 32.—Two photomicrographs; the first ( $\times 25$ ) is of a section of a nodule on the anterior wall of the stomach caused by the encapsulation of food (oatmeal) escaping through a perforated duodenal ulcer, and the second ( $\times 60$ ) is of an implant on the under surface of the diaphragm secondary to cancer cells escaping into the peritoneal cavity from an ovarian cancer (see Figs. 1 and 43 of a previous paper<sup>1</sup>). The reactions caused by these foreign bodies lodging on the surface of the peritoneum are identical with those shown in Fig. 31. Therefore we are tempted to designate at least some of the encapsulated patches of cancer and müllerian epithelium on the surface of the peritoneum as implantations of foreign body type.

the implantation, in this situation, of epithelium escaping from the uterine cavity or from endometriosis of the ovary? If so, it is impossible to detect the place of fusion of the surface epithelium of the implant or graft with that of the tubal mucosa of the fimbria.

Is primary fimbrial endometriosis the result or the cause of the pelvic endometriosis usually present in such cases? In one instance the only endometriosis found, other than fimbrial, was situated in the tubal wall beneath the differentiated mucosa of the tubal fimbria and apparently

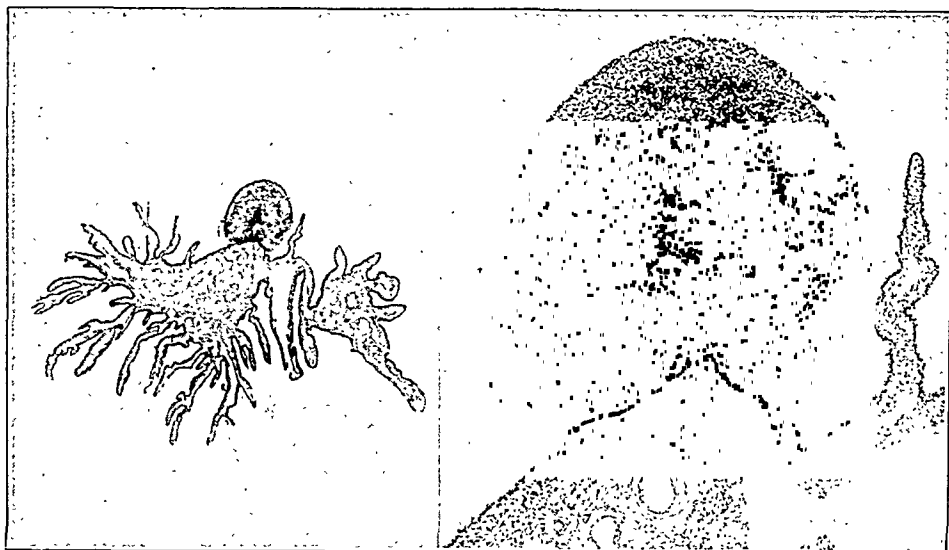


Fig. 33.—Two photomicrographs, the first ( $\times 8$ ) is of a cross section of a portion of the fimbriae of the right tube showing a small nodule of granulation tissue on the palmar surface of the fimbria (Case 10). The second is of a ( $\times 45$ ) magnification of the nodule shown in the first photomicrograph. There has been a loss of epithelium at the origin of the granulation tissue from the fimbria. Many such nodules were present on the palmar surfaces of the tubal fimbriae (see Fig. 40). None were observed on the fimbriae of the left tube: they might have been missed as the tube was not removed. A similar but larger patch of granulation tissue was found arising from the mucosa of the ampulla of the right tube which was first thought to be a fragment of endometrial tissue and so described. The patient had peritoneal endometriosis and was operated on the second day of her menstrual period. I do not know the significance of the localized areas of granulation tissue.



Fig. 34.—Photomicrograph ( $\times 8$ ) of a longitudinal section of the fimbriated end of the left tube through its lumen (Case 11). Endometriosis "Imp." is present on the surface of the tube distal to the base of the fimbriae (see Fig. 35).

Fig. 35.—Three photomicrographs demonstrating a possible origin of the endometriosis shown in Fig. 34. The first ( $\times 60$ ) is of the fimbrial mucoserosal junction proximal to the endometriosis mentioned above and from the same section. Normal fimbriae are shown above covered by tubal mucosa. However, there is an evident loss of some of the epithelium covering the terminal portion "Ter. p. m." of this mucosa. The serosal surface of the tube is covered by mesothelium, the cells of which are higher than normal in this situation but do not resemble the tubal epithelium. A gap between the terminal portion of the tubal mucosa and that of the mesothelium is partially filled with granulation tissue. From this area an exudate (see arrow) is

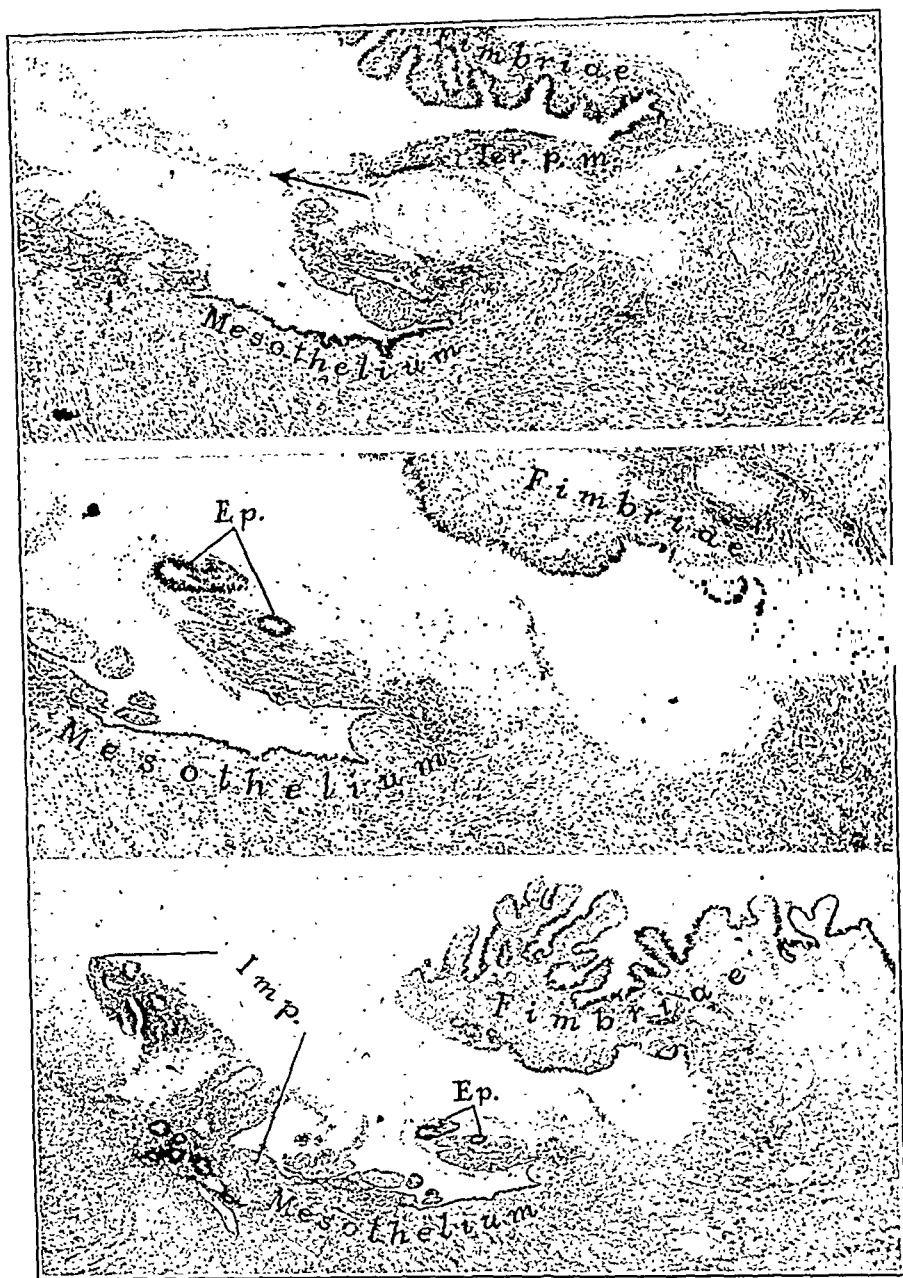


Fig. 35.

escaping into the peritoneal cavity and might have carried epithelium with it. The second photomicrograph ( $\times 60$ ) is of the same area shown above, at a different level, but very near the preceding section. One can readily see the structures shown in the first section, namely, the fimbrial mucosa covered by epithelium and the serosa by mesothelium. There has been evidently a loss of epithelium. The surface of this raw area is covered by an exudate with two gland-like inclusions of epithelium "Ep." the upper one is enmeshed in fibrin and the lower one partially embedded in granulation tissue. I am tempted to infer that the epithelium forming these glands was cast off from the terminal portion of the fimbrial mucosa as indicated in this and the first photomicrograph, and that later it might give rise to a patch of endometriosis "Imp." similar to that in the third photomicrograph. This last photomicrograph is ( $\times 25$ ) a magnification of the section shown above and including the area of the latter. Three stages are represented in the development of this implant "Imp." the escape of epithelium from the terminal portion of the fimbrial mucosa, the fixation of the epithelium in fibrin, its embedding in granulation tissue by the organization of the fibrin and finally the finished implant which is of the foreign body type.



arose from the latter by direct extension (see Case 4 and Figs. 13 and 14).

This case and others reported in this paper (see Cases 3, 5, 6, and 7) have convinced me that primary fimbrial endometriosis, at least in some instances, is the cause of the associated pelvic endometriosis.

It has been shown that müllerian epithelium carried with menstrual blood may escape from or through the tubes into the peritoneal cavity from the following sources:

1. The mucosa lining the uterine cavity.
2. The mucosa lining the tube, as suggested by the incidence of hemosalpinx in patients with pelvic endometriosis when the fimbriated ends of one or both tubes are occluded and also by the presence of patches of uterine mucosa in patent tubes.
3. Primary fimbrial endometriosis.

Can epithelium be disseminated into the peritoneal cavity from tubal fimbriae by any other phenomenon than the menstrual reaction of a primary tubal endometriosis? In Case 10 (see also Figs. 33 and 41), small areas of granulation tissue were found on the palmar surface of the tubal fimbriae of a patient with pelvic endometriosis operated upon during her menstrual period. I have recently encountered a like case occurring under similar conditions. I do not know its significance, but it indicates that there must have been a loss of tubal epithelium over these areas.

During the study of tubal stumps, endometriosis was found occasionally in the stump or in structures adherent to it, which was shown not to be continuous with the mucosa of the stump. These were interpreted as having possibly arisen from the growth of tubal epithelium transplanted by the surgeon at the original operation, unless they were present prior to that operation. If tubal epithelium transplanted by the surgeon sometimes grows and becomes differentiated into mucosa of uterine type, we would expect that tubal epithelium escaping from the fimbrial mucosa as the result of nonoperative trauma other than the menstrual reaction of fimbrial endometriosis might do the same. The

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Fig. 36.—Painting of a lateral view of the right tube, mesosalpinx and ovary (Case 1) showing primary fimbrial endometriosis "c." arising in tubal mucosa which had spread over the surface of the mesosalpinx from the base of the ovarian fimbriae (see Figs. 6 and 7).

Fig. 37.—Painting of the fimbriated end of the right tube and a portion of the wall of an endometrial cyst beneath it (Case 2). Two patches of endometriosis "c." are shown. The upper one is a primary fimbrial endometriosis (Figs. 8 and 9), and the lower one is probably a secondary endometriosis of implantation origin.

Fig. 38.—Painting of a lateral view of the right tube, mesosalpinx and ovary (Case 3) showing a primary fimbrial endometriosis "c." with invasion of the mesosalpinx (see Figs. 10, 11, and 12).

Fig. 39.—Painting of the fimbriated end of the right tube with multiple hemorrhagic fimbriae due to an early menstrual reaction in primary endometriosis of these fimbriae (Case 4, see Figs. 13, 14 and 15). The patient (Case 11) was operated upon twelve hours after the onset of menstruation. An accessory fimbrial opening is present proximal to the main one.

Fig. 40.—Painting of a posterior or mesial view of the right tube and ovary (Case 8). The ovary containing an endometrial cyst is turned upwards exposing the opening in its lateral wall caused by freeing the ovary at the operation. The primary fimbrial endometriosis (Fig. 29) is situated at the base of the ovarian fimbriae. The patient was operated upon in the interval stage of the menstrual cycle.

Fig. 41.—Painting of the fimbriated end of the right tube (Case 10) showing small nodules of granulation tissue on the palmar surfaces of the fimbriae. The patient was operated upon the second day of her menstrual period. The bright colored nodules (Fig. 33) are of recent origin possibly due to the present menstrual reaction. The grey colored nodules on the upper fimbriae may represent a later stage of the others, possibly caused by a previous menstrual reaction.

possibility of this is suggested in the study of the reactions occurring at the mucoserosal junction, where one frequently finds evidence of the loss of the epithelium (Fig. 3), or of its having been embedded in adjacent tissues (see Fig. 4). This possibility is strengthened by the condition found in Case 11 (see also Figs. 34 and 35 and their legends).

#### SUMMARY

Primary fimbrial endometriosis develops from the activation and differentiation of the tubal mucosa of the fimbriae into a structure (growth) resembling endometrium. A like condition may arise in the mucosa of the ampulla of the tube. These are distinct pathologic entites which may be grouped with primary uterine endometriosis (uterine adenomyoma of mucosal origin and adenomyosis interna), primary endosalpingiosis and endometriosis arising from the mucosa of the proximal portion of the tube, postoperative endometriosis continuous with the uterine mucosa and also postsalpingectomy endosalpingiosis continuous with the tubal mucosa. They should not be grouped with the various forms of misplaced müllerian mucosa not in continuity with the mucosa lining the uterus and tubes.

I realize that all misplaced müllerian tissue derived from tubal mucosa, etiologically, should be designated as endosalpingeal, but when it becomes differentiated into a structure resembling endometrium I am tempted naturally to call it endometrial.

Primary fimbrial endometriosis may invade or spread over the surfaces of the wall of the tube and mesosalpinx. When it arises in ovarian fimbriae it may likewise involve the ovary and even cause endometrial cysts of that organ. This differentiated mucosa reacts to menstruation and since it is exposed (unencapsulated) to the peritoneal cavity, menstrual blood, carrying with it bits of müllerian tissue, readily escapes into the pelvis. This disseminated tissue should possess the same potentialities of implantation as similar tissue escaping from ovarian endometriosis. Primary fimbrial endometriosis, therefore, is one of the varieties of endometriosis from which pelvic endometriosis in other situations may arise by extension and dissemination. The frequency and importance of this variety in the life history of pelvic endometriosis has not been determined.

Primary endometriosis probably arises in any part of the fimbrial mucosa. In my experience it has developed in the terminal portion of this mucosa at or near the mucoserosal junction, in all instances in which I have been able to determine the exact site of its origin. The abrupt termination of the tubal mucosa at this point, often with a definite gap between its epithelium and the mesothelium of the serosa, constitutes a vulnerable and unstable area. This is manifested by evidence of injury or stimulation with loss of epithelium and reactions indicating repair of an injury, even in normal appearing tubes. The conditions found in this situation may resemble those encountered in the re-

pair of the mucosa in the severed ends of salpingectomy stumps. I believe that trauma and repair of injured tubal mucosa constitute important factors in the etiology of endometriosis at the mucoserosal junction of tubal fimbriae and in and about salpingectomy stumps.

A study of conditions often present at the mucoserosal junction, other than endometriosis, indicates that epithelium is sometimes disseminated from the terminal portion of the fimbrial mucosa by reactions, the cause of which I do not fully comprehend. Could this extruded epithelium possibly cause endometriosis by implantation? This is only one of the many unsolved problems relating to pelvic endometriosis.

Many data have been collected which should be considered in determining the etiology of müllerian mucosa on the surfaces of the ovaries and peritoneum. A few of them I wish to enumerate and some I shall discuss briefly.

1. The frequency of tubal patency and the incidence of hematosalpinx when one or both tubes are occluded.

2. The distribution of the early lesions in situations accessible to material escaping from the tubes and in sites where this material might be retained.

3. Their character, often indicating a local reaction to an injury caused by some foreign body and the repair of that injury.

4. The significance of menstrual blood both in the etiology and dissemination of pelvic endometriosis.

5. The structure of the epithelial "growths" in these lesions is the same as that of the tubal and uterine mucosa from which the material causing the lesions was derived.

6. The lesions of pelvic endometriosis, including ovarian, and endometrial cysts not in continuity with the tubal mucosa, are similar to those arising from the invasion of these structures by the activated mucosa of tubal stumps and of primary fimbrial endometriosis, the only difference being a break in continuity between the müllerian mucosa in the primary and secondary situations. By what phenomena can the spanning of this break be explained?

7. The various stages in the development of peritoneal endometriosis correspond with similar stages in the development of peritoneal carcinomatosis of accepted implantation origin.

Both uterine and tubal epithelium at times escape through patent tubes from müllerian mucosa, a tissue frequently possessing the invasive traits of cancer. Tubal and uterine epithelium sometimes becomes activated as the result of trauma and repair, causing endometriosis under these circumstances (tubal stumps, mucoserosal junction of fimbriae and incised wound of the uterus). Therefore I believe it possible that a similar repair of injury, arising from the traumatized (and therefore sometimes activated) epithelium escaping from or through patent tubes, may result in endometriosis on the surface of the various pelvic structures on which this activated epithelium lodges. Occasionally similar lesions apparently arise from müllerian epithelium transplanted during operations on the tubes and uterus.

On the other hand the supporters of the metaplasia theory for the

origin of pelvic endometriosis other than that in continuity with the mucosa lining the tubes and uterus, may claim that I have given them excellent ammunition with which to shatter the implantation theory. Since tubal mucosa may become differentiated into endometrium-like tissue, it is their privilege to assert that mesothelium and the surface epithelium of the ovary, also derivatives of the celomic epithelium, could become differentiated into either uterine or tubal mucosa if activated by the proper stimulant and that such a stimulant may be present in material escaping from or through the tubes. Sometimes endometriosis on the surface of the various pelvic structures is not encapsulated and closely resembles the differentiated mucosa of a primary fimbrial endometriosis, hence why not a primary mesothelial endometriosis in such cases? I would expect that this might occur in patches of tubal mucosa should the latter be present in these situations. I have demonstrated this phenomenon in tubal epithelium which had spread over the surfaces of the tube, mesosalpinx and ovary from the fimbriae. We must not lose sight of the fact that a similar type of lesion also occurs in peritoneal carcinomatosis and that the surface of skin grafts, even very small ones, is uncovered.

The general laws governing the healing of wounds of the various structures and organs are the same whether caused by the surgeon or by disease. A comparative study of peritoneal endometriosis and peritoneal carcinomatosis demonstrates that in each one sees the histologic structure of the parent tissue (müllerian mucosa in one instance and cancer in the other) from which they have arisen as the result of something escaping into the peritoneal cavity. The same study convinces one that not only are the histologic pictures of the various stages in the development of the peritoneal lesions in the two conditions similar but also their end results. Therefore one is tempted to believe that the fundamental method of origin of the secondary growths is the same in each instance.

If endometriosis arises from a differentiation of the mesothelium due to some stimulant escaping through the tubes we well might infer that peritoneal carcinomatosis might arise from a differentiation of the mesothelium caused by some substance escaping from the parent cancer. Even if this be true, as is possible in some instances, it does not prove that all of the lesions of peritoneal endometriosis and carcinomatosis arise in this manner and that implantation is not the chief method of their origin. Our present conception of metastatic cancer is based on the transplantation (implantation) of cancer cells escaping from the primary tumor.

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NOTE: The paintings from which the color plate was made, which portray primary fimbrial endometriosis far better than any verbal description, were made by Mrs. M. R. Marden. The photomicrographs were made by Mr. James A. Glenn. The demonstration of the origin and extension of these lesions was greatly facilitated by the technical skill and care of Miss Isabel Peck. Dr. Victor C. Jacobsen made valuable suggestions and criticisms. These I thank for their interest and cooperation.

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## THE DIAGNOSTIC VALUE OF RADIOPAQUE CONTRAST MEDIA IN GYNECOLOGY AND OBSTETRICS\*

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THE beneficent discovery of the roentgen ray in 1895 has illuminated practically every field of medicine. In gynecology and obstetrics, both from a diagnostic and therapeutic standpoint, it has been of immeasurable value.

It is interesting to note that in gynecology the x-ray was first used as a therapeutic agent and later employed for diagnostic purposes, while in obstetrics it was first used as a diagnostic measure, and even today its use as a therapeutic agent has no rational basis.

There is some doubt to whom credit should be accorded for the conception of introducing radiopaque contrast media into the genital tract for purposes of roentgen diagnosis. Cary, of our own country, published the first report in March, 1914, while Rubin published his observations in May of the same year. Dartigues and Dimier of France maintain that they used it before that date, but because of the war were unable to publish their results until 1916.

The question of precedence is of little consequence, but the use of contrast media in the genital tract was epochal, and gynecologists soon saw the possibilities of diagnostic achievement, in the hope that an innocuous radiopaque substance could be found with which gynecologic diagnosis could approach, and even exceed, in accuracy that which has been accomplished by the use of barium in the gastrointestinal tract.

Since 1914, when Cary and others used collargol, various other radiopaque substances have been introduced into the genital tract for diagnostic purposes. Among those were sodium bromide, sodium iodide,

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strontium iodide, lithium iodide (umbrenal), bromide oil, bromized oil (contrastol), rapeseed oil (campoidal), etc. With few exceptions these preparations proved to be objectionable because of their irritating and toxic qualities. Some serious complications and even fatal results have been reported following the exhibition of these preparations. It was not until 1925 that Carlos Heuser, of South America, reported the first use of lipiodol in his sterility studies and in the early diagnosis of pregnancy.

Since the use of lipiodol in the field of gynecologic diagnosis, there has appeared a voluminous amount of literature concerning it. After a careful survey one comes to the conclusion that, in a general way, lipiodol is, at the present time, the preparation of choice. After its use in thousands of cases by gynecologists from many different countries, one cannot escape the conclusion that this preparation, which is so impermeable to the x-ray, is nonirritating, nontoxic, and that it can be administered with a minimum amount of discomfort and danger to the patient.

One may state today that lipiodol is a standard preparation which is being used in uterosalpingography and that all other radiopaque substances have been largely abandoned because of their irritating and toxic qualities.

Irving S. Stein, who has had a large experience with x-ray pneumoperitoneum, has used lipiodol in conjunction with it in over two hundred cases, and he believes that the combination of these two procedures is of striking diagnostic value in gynecology and obstetrics.

It is not the purpose of this presentation to discuss the merits of gas insufflation as compared to those of radiopaque media in gynecology and obstetrics. The original, brilliant, and exhaustive amount of work which has been done by Rubin on uterotubal insufflation is of monumental significance; and it has associated his name with the extensive literature on sterility and tubal impermeability. The writers believe that both tubal insufflation and uterosalpingography have their proper place in the diagnosis of abnormalities of the genital tract. Many gynecologists use both methods, many favor the Rubin method, while many others, especially the French school, favor the radiopaque injection.

The senior writer can only state that after acquainting himself with the technic of tubal insufflation and following its practice for a period of five years, he has practically abandoned it in favor of lipiodol injection, and that during the last five years he has rarely done a gas insufflation. While the writer had no untoward occurrences as the result of tubal insufflation, except in one case of ectopic pregnancy, which he does not believe can be proved to be the result of the insufflation, he believes that in his own personal experience, lipiodol has proved much more satisfactory than the Rubin method, and that results which he has obtained from its use are more positively informative than those which were obtained by the use of gas.

When in the field of gynecology and obstetrics a comparatively new diagnostic procedure is suggested, which involves the entrance of a foreign substance into the inner genitalia, which nature has guarded with certain defense barriers, the physician's natural reactions suggest the following questions:

1. What is the danger attending such procedure?
2. How much pain and disability will this measure cost the patient?
3. Has the test been done in a sufficient number of cases, and with such a satisfactory technic that conclusions of value may be drawn from it?
4. What information can be obtained that cannot be gained by a careful gynecologic examination, made under anesthesia if necessary?
5. Can its field of usefulness be extended toward more precise diagnosis in gynecology and obstetrics?

The dangers attending uterosalpingography, assuming the use of a proper technic, are practically always avoidable, granting that the physician carefully examines the patient and excludes all cases who present the following conditions:

1. Active genital tract infection.
2. Leucocytosis and fever.
3. Recent extensive uterine bleeding.
4. Premenstrual, comenstrual, and immediate postmenstrual periods.
5. Pregnancy, normal and extrauterine.
6. Any disease rendering a patient acutely ill or any severe constitutional ailment.

The danger of introducing a foreign body into the genital tract in the presence of active infection is too obvious to require more than passing comment; the possibility of forcing organisms and infectious material through the fallopian tubes into the peritoneal cavity must be ever present when performing a uterosalpingography. Local peritonitis, general peritonitis, and deaths have occurred from this procedure and undoubtedly will occur if the greatest care is not exercised, and especially if this work should become a current practice among physicians who are not trained gynecologists.

A microscopic examination of the vaginal and cervical flora should precede every examination.

Inasmuch as this test is never an emergency measure, no patient should be submitted to it when there is any suspicion of the presence of infection or other unfavorable condition. It is much better to wait for weeks, if necessary, than to awaken an infection that may last for several months.

If the patient has had a recent, extensive uterine hemorrhage there is danger of infection and there is a possibility of oil embolism. Furthermore, there is danger of improper interpretation of the roentgenogram which might be occasioned by the presence of blood clots.

Early in this work it was suggested by Rubin, and verified by others, that the mucous membrane of the inner genitalia is more suitable for gas insufflation and for uterosalpingography from five to ten days after

completion of the monthly period. At this time there is less danger of infection, less danger of physiologic blockage and there is more probability that there will be a more normal physiologic response of the uterus and tubes to the opaque media.

One of the definite contraindications to the use of uterosalpingography is pregnancy, notwithstanding the fact that Heuser and several other observers made the statement early in this work that it will not result in abortion.

It is obvious that no intelligent physician would submit any sick woman (irrespective of the nature of her illness) to this delicate test which, under the most favorable circumstances, is only practiced on a comparatively small group of women.

The introduction of radiopaque media into the genital tract always produces some discomfort to the patient. However, with the use of fresh, clear, and warm lipiodol and by the use of a standardized technic in which the utmost gentleness and delicacy are employed, pain is negligible, in a woman possessing an ordinary, stable nervous system. In our own work we rarely employ a narcotic preceding, during, or following the test.

Our patients are required to remain in the Clinic for about eight hours during the first day of the test, and to return in twenty-four hours for a control picture, which can be made in a very few moments.

What information can be obtained from the above test that cannot be gained by a very careful gynecologic examination, made under anesthesia, if necessary?

The supreme diagnostic value of the use of radiopaque media in the genital tract is that it gives us precise information as to the patency or nonpatency of the fallopian tubes and the location of the blockage when present. In cases of sterility, where the most careful bimanual examination made by the most competent gynecologists fails to reveal tubal pathology, even with the patient under an anesthetic, this test finds its greatest usefulness.

Until tubal insufflation and salpingography were introduced there was no way of ascertaining the presence or absence of tubal blockage without opening the abdomen, and even then the information that was obtained was not as reliable as that which can be obtained by uterosalpingography. Many hundreds of cases have been checked on the operating table to prove the accuracy of salpingography. Comparisons have also been made at autopsy in verification of the dependability of this test.

In fact, if this measure never accomplished any more than the diagnosis of the presence and the location of organic tubal obstruction, with the added number of cases of pregnancy that have followed it, it will be considered as one of the most notable gynecologic accomplishments during the last quarter of a century.

While errors of interpretation in uterosalpingography have occurred



and will occur, these errors will be reduced to a minimum as the work proceeds. When a standard technic becomes a matter of general practice and when the roentgenograms from the various Clinics are compared, the use and dependability of the test will be gradually extended.

It seems to the writers from an extensive review of the literature, and from their own personal experience, that a most attractive field of investigation challenges the gynecologists and radiologists who should work in the closest cooperation in this comparatively new field of diagnosis.

In addition to its value in determining the presence and location of tubal occlusion, uterosalpingography offers itself to the following conditions, in a practical way:

1. Exact size, shape, contour, and tonicity of the uterus.
2. Presence of intrauterine tumors.
3. Presence of adnexal tumors, such as hydrosalpinx, ovarian cysts, etc.
4. Presence of salpingian adhesions due to extragenital pathology.
5. Presence of anomalies of uterine and tubal development.
6. Differentiation between the genital tract pathology and that in the region of the cecum and sigmoid.
7. Diagnostic check on results of tubal reparative surgery.

Radiopaque contrast media may be introduced into the genital tract for diagnostic purposes either by the open or the closed method. Dyroff advocated a very slow, drop by drop, introduction, leaving the cervical canal open, and he observed that the tubes became filled, not from the pressure but from uterine contraction. He observed through the fluoroscope the contrast medium running out of the tubes, drop by drop, toward the lateral pelvic walls, and he demonstrated that the oil was driven by the tubes into the peritoneal cavity. He was the first to show by films the segmented filling of the tubes, which gives the appearance on the films of a string of beads. About the same time that Dyroff made this observation, others such as Gregoire, Darbois, and Bécélère observed that the tubes dilate and contract irregularly.

Schneider and Eisler observed that in the closed method, when the media is introduced, the uterus contracts in various ways, and they stated that the oil is driven to its destination by uterine contraction and tubal peristalsis. They noticed the disappearance of one uterine horn while the opposite one dilated; they also noted alternating changes in form of the fundus. They stated that, under the fluoroscope the media forms a round or pear-shaped shadow, and after the fundus becomes filled, the isthmus becomes filled, making a funnel-shaped shadow. In a few minutes the tubes are filled in their whole course. Schneider and Eisler believe that this is a physiologic response of the uterus and tubes to the contrast media.

These authors suggest that in hysterosalpingography the function of the fallopian tube may be studied in relation to ovulation and that, as a result of these researches, some therapeutic measures may be forthcoming. They suggest that these studies may help in an understanding in both the function of the tubes and the physiology of gestation. They warn, as do other authors, about the danger of misinterpretation of findings as regard shadows due to other conditions, such as phleboliths, vesical, and ureteral stones, calcified ovarian and calcified fibroid tumors, and dermoid cysts with bone formation.

Schultz, in considering the basis of hysterosalpingography, states that constitu-

tional conditions of the uterus determine its response to a filling media. In an atonic uterus, for instance, the angles are rounded and the definitely triangular figure seen in the normal condition, is missing; therefore, it requires more media to fill the cavity. Schultze states that a normal sized uterus generally does not require more than 7 c.c. to fill it, and if it then fails to show a clean-cut triangle, with sharp corners, one may assume that there is a uterus with decreased tone and a yielding wall. He states, however, that there are variations in the form of the uterus which are within normal limits and that unless one has a complete filling the tubes may not fill and erroneous interpretations are possible.

Schultze says that it is essentially the contraction of the uterus which fills the tubes with contrast media, and he has observed that the two tubes do not fill synchronously, in the majority of cases.

He distinguishes three stages of the filling process of the tubes, the first state is the passage of the oil from the uterus to the ampulla, which occurs very rapidly, so rapidly that one seldom sees it; the second stage represents a slight delay of the oil at the fimbriated end; and the third, the passage of the oil through the fimbriated extremity into the peritoneal cavity.

He believes that the transport disturbance of the tube may be due to adhesions or inflammatory thickening of the wall but thinks that an impermeability can exist on a purely functional basis. He warns that the true diagnostic value of this test will only be attained after a long comparison of films and by following the clinical course of cases and by laparotomy findings.

Schultze suggests that our aim in the future should be toward determining how much negative films rule out pathologic changes.

We believe that in the future some radiopaque medium may be discovered that will permit of a more positive detail than that which can be obtained by lipiodol, and thereby make negative film findings more positively exclusive of tubal pathology.

In our own work we have observed how rapidly the uterus will sometimes propel the opaque media into the abdominal cavity, and we believe that during a process of filling the uterus one film should be taken. On the other hand, sometimes the oil remains in the uterus for an hour or two, if not longer, before entering the tubes. We, therefore, believe that to avoid error of interpretation, films should be taken during the filling process and at various other intervals, and that the cervix should be kept closed for a considerable time after the introduction of the media.

Reinberg and Arnstam state that they have discovered, by use of radiopaque media, some important facts concerning the anatomy and physiology of the fallopian tubes; they say that the fluoroscope may play only an unimportant rôle in this work, that the cinematograph is not yet perfected, and that, at the present time, the repeated taking of films is the most practical. They believe that the form of the uterus depends on the muscular tonicity and the position of this organ in the pelvis. They believe that the usual capacity of the uterus is from 3 to 4 c.c., while the hypoplastic type may have a capacity of only 2 to  $2\frac{1}{2}$  c.c.

These authors state that lipiodol under slight pressure produces a tonic contraction of the uterine walls. After introduction the lipiodol gathers around the end of the cannula and forms a spindle, and that after the addition of a larger amount, the expanding shadow takes the form of an isosceles triangle. This triangular shadow is characteristic of normal muscular tone and when a tonicity is present the cornua have rounded instead of angular corners. It seems as if the uterus, in an effort to rid itself of the contrast media, squirms and assumes various shapes, such as have

been described by Schneider and Eisler, Schultze, Reinberg and Arnstam, and other authors.

Reinberg and Arnstam describe a pendulum-like movement of varying amplitude, while the uterine wall moves upward and downward, and even tetanic movements have been noted. When the uterus is permitted to empty its contents into the vagina, the contractions may be rapid and jerky; they may occur immediately or they may be delayed.

When the uterus contracts metrosalpingographic observations show that the lipiodol is pushed into the abdominal cavity drop by drop as has been demonstrated under the fluoroscope. While there is some arrest at the fimbriated extremity, it is usually driven rapidly into the vagina. Reinberg and Arnstam state that they have discovered a sphincter at the uterine end of the tube, and Arnstam has obtained a photomicrograph of the same. These authors state that under normal conditions, the uterine and tubal cavities are either completely or partly shut off by contraction of muscular fibers, which are buried in the interstitial portion of the tube. When there is not a complete contraction the lipiodol may be seen like a thread connecting the two cavities. They believe that changes in the lumen described above are brought about by local, tonic contraction of the circular muscular fibers. These authors also suggest that uterosalpingographic studies may help to understand how the ovum is transported, and the part that tubal peristalsis plays, compared to the rôle played by the ciliated epithelium. Their studies with contrast media in the tubes lead them to believe that these organs are extremely movable, and that under normal conditions they change their form and position.

Reinberg and Arnstam state that their films have demonstrated clearly both an active peristalsis and an antiperistalsis, and that while the contrast media may be pushed toward the uterus, and also toward the fimbriated extremity, the usual peristalsis is from the cornua to the abdominal end. They believe that the tube plays more than a passive rôle in furnishing a transport tunnel and that there is a definite peristaltic contraction of the musculature present. They agree with other observers that the segmented, beady appearance of the tube as seen through the fluoroscope and on the film is due to peristaltic tubal activity.

Schultze, quoted by Cotte, states that there are two kinds of uterine contractions, namely, partial, in which different segments of the uterus function independently of each other, and which may be demonstrated by x-ray films taken in series; and second, complete contraction, due to the simultaneous operation of the body of the uterus and the horns.

From the standpoint of interpretation, Cotte suggests that one should keep in mind certain important points, namely, that the tubes cannot usually be seen in their entire course, excepting when they are obliterated at the fimbriated end; that the tube usually goes out from the uterus in a horizontal line; that in the isthmus, the contrast media looks like a filiform streak; that the situation of the tubes varies; that they may be situated low in the pelvis or suspended by reason of adhesions; that they are often folded and bent back upon themselves. And furthermore, that some uteri are hyperkinetic to the extent that as soon as the medium is introduced they expel it immediately, while other uteri may be so atonic that they hardly react to any amount of distention.

Nahmacher has observed that ordinarily the pressure in the uterus is not sufficient to force the fluid through the entire tube, especially since the ampullar end is but little dilated, and he, therefore, concludes that there must be active peristaltic action of the tubes toward the peritoneal cavity.

Jarcho states that, if the films are taken in series, one may find that the tubes are not filled at all, while in others they are filled in their entirety; or that they are filled only at the proximal end, or only at one of the distal portions. He further states that when tubes are not filled it may be due to insufficient contrast media in the

uterus, atony of the uterus, or spasmodic contraction of the cornua, or of the proximal portion of the tube. He and others have observed that even a few drops of the contrast medium introduced into the uterus will sometimes find their way into the tubes.

Schultze, studying the phenomena of uterosalpingography, devised a method by which he could take six serial views in a half a minute, and at the same time he watched the progress of the opaque medium and the behavior of the uterus and tubes. By this method he could change from screen to film and from film to screen as often as he wished. In this way it was possible to observe that the same uterus gave different shadows according to the amount of its filling.

Petit-Dutaillis states that adhesions of the tube, due to extragenital causes, such as appendicitis, can, by salpingography, be located and proper treatment instituted in certain cases of sterility, and that in these cases practical information can be obtained which cannot be gained in any other way.

The writers desire to make a plea for a more general standardization of the whole procedure, from the following standpoints:

1. Time of administration relative to menstruation.
2. The amount of contrast media used.
3. Routine use of the manometer.
4. Definite intervals between the taking of roentgenograms.
5. A control film always taken twenty-four hours after introduction of the contrast media.

The authors make the following recommendation in the above connection: First, the time of administration should be approximately one week following the cessation of the last menstruation and coitus should be interdicted meantime. Second, the amount of contrast media should be about 5 to 7½ c.c. Third, the introduction should be under the control of a manometer and the pressure should not exceed 250 mm. of mercury. Fourth, the first film should be taken during or immediately after the filling of the uterus, a second one ten minutes later, the third an hour later, a fourth four hours later, and a fifth at the end of twenty-four hours. Anteroposterior exposures should be frequently supplemented by roentgenogram in profile. We have found that a slightly oblique position instead of a true lateral is desirable.

Cornell and Warfield state that in the Cook County Hospital in Chicago the x-ray examinations have been made of all urinary complications during pregnancy and the puerperium. It is well known that normal woman during pregnancy, without any complaints, show a marked dilatation of the right ureter. Cornell and Warfield found that the left ureter showed a much less degree of dilatation but that the right one showed evidence of it from the third month on. These authors used skiodan, 20 gm., dissolved in 50 c.c. of sterile water. Films were exposed in ten minutes, thirty minutes, one hour, and four hours after injection. They found that the pathologic kidney is slow to visualize as compared to the normal and it retains the opaque material much longer. Cornell believes that the visualization of the urinary tract in normal pregnant women may show that accepted facts will have to be revised; these authors bring out the fact that this test offers a means of confirming urinary tract disease diagnosis without great discomfort to the patient and helps in a decision whether or not a patient should be examined with a cystoscope or catheterized. This method of kidney and ureter visualization marks another triumph for radiopaque media in the field of obstetrics.

The use of opaque media in obstetrics has received little attention from the profession at large. Except for the occasional use of lipiodol in the early diagnosis of normal and extrauterine pregnancy, no references were found in the literature in 1930. A study made in that year by some of us led to the use of contrast media in patients at or near term. Some interesting results were obtained. It was found that a water-soluble contrast medium could be injected into the amniotic sac with relatively little danger. The purpose of this study was to outline, if possible, the site of implantation of the placenta. This was found to show as a filling defect on the film.

The method employed involved the injection of an aqueous solution of strontium iodide prepared in the following manner: Ten grams is placed in a sterile flask with about 15 c.c. of sterile distilled water and brought to a boil. This dissolves the strontium iodide and at the same time a trace of an easily filtered precipitate of strontium carbonate may be thrown down. This precipitate is filtered off through sterile filter paper and a sterile funnel, into a second flask. The solution is then boiled slowly for ten minutes; it is allowed to cool and then is ready for injection.

The bladder is emptied. Careful palpation of the abdomen is used to determine the position and presentation; the position and rate of the fetal heart are recorded; the abdomen is carefully cleansed with iodine and alcohol from the umbilicus to the symphysis. Sterile towels are draped around this area; the operator puts on sterile gloves; a few cubic centimeters of one-half per cent novocaine is injected under the skin just to the right or left of the mid-line about halfway between the umbilicus and symphysis. The injection is usually made on the side where the fetal small parts are felt. A *nineteen or twenty gauge Pitkin needle*, with a stylet, is used. This needle is of the type that will bend without breaking and is used in spinal puncture work. The needle is inserted through the anterior abdominal and uterine walls. When the amniotic sac is entered a distinct snap is felt, as in doing a spinal puncture. The stylet is withdrawn. Very frequently amniotic fluid will flow back through the needle; sometimes blood is encountered. This is probably due to the fact that the point of the needle is in the placenta and one should insert the needle still farther.

A 10 c.c. syringe is now attached to the needle and the amniotic fluid withdrawn in an amount which is approximately equal to the amount of strontium iodide solution which one intends to inject. The strontium iodide solution is taken in a twenty or thirty cubic centimeter syringe and attached to the needle in the amniotic sac and amniotic fluid is withdrawn. This serves two purposes, one to be sure that the needle is in the amniotic sac, and the second to cause some dilution of the concentrated strontium iodide solution in the syringe. The iodide solution is injected and fluid is withdrawn alternately so that at no time is a large amount of concentrated solution being put into the amniotic sac.

When injection is completed the needle is withdrawn and a small sterile dressing applied, and the patient is instructed to lie on the left side for ten minutes, on the right side for ten minutes, and then on the back. This allows a diffusion of the strontium iodide through the amniotic fluid. The first x-ray is lateral, with technic as follows: *one hundred ma., 80 to 85 K.V.P., time—three seconds on the Bucky*; the patient is then turned and a posteroanterior is taken, with a hundred ma., 85 to 90 K.V.P., time—three seconds. An oblique is taken with about the same factors as is used on the P.A.

Certain observations of considerable theoretical interest have been made, including the fact that the infant swallows amniotic fluid in suf-

ficient quantities to outline the stomach and intestinal tract, the determination of loops of cord about the neck, and occasionally the determination of the sex of the fetus when the buttocks happens to appear in profile.

Two observations, however, appear to be of considerable practical importance: First, it is possible to obtain a distinct outline of the soft parts and in this way accurately estimate the relative size of the fetus and, thereby any disproportion, if such exists. Second, it offers a precise method of locating the placenta in cases of silent bleeding, without the usual dangers of contamination, attendant on vaginal examination.

At a meeting of this Society two years ago the senior author, in discussing Dr. Matthews' paper on the roentgen ray as an adjunct in obstetric diagnosis, referred to this work and stated, that the pictures in these cases were a great improvement on the ordinary film. He also stated that the work was not entirely devoid of danger and that it was too early to predicate the practicability of it, but that it was of extreme academic interest.

Certain physicians have reported a high fetal death rate following attempts at amniography. Careful investigation revealed the fact that these physicians were using, not strontium iodide, but sodium iodide. From our experience we believe that the use of sodium iodide in this work is dangerous and distinctly contraindicated.

We feel that it is imperative that the greatest care should be exercised in the preparation of the solution, using only a chemically pure drug. Only a fresh solution should be injected. The average dose varies from 7 to 10 grams, according to the estimated size of the uterus and should not be exceeded. Proper selection of cases is advisable, remembering, that its chief value lies in cases of bleeding without contractions.

#### CONCLUSIONS

1. Radiopaque contrast media, used for diagnostic purposes in the field of gynecology and obstetrics, is a valuable adjunct to a careful history and a careful pelvic examination; it promises to lead the way to a broader field of accurate diagnosis.

2. In gynecology, at the present time, lipiodol is the contrast fluid of choice because of its radiopacity and because by following a proper technic in selected cases, its use is practically without danger and causes little discomfort to the patient.

3. Hysterosalpingographic studies have added to our knowledge of the physiology and anatomy of the uterus and tubes.

4. A suggestion has been made for a more general standardization of technic so that roentgenograms from the various Clinics may be compared in an effort to achieve more accurate interpretation.

5. The use of radiopaque media for the visualization of the genito-urinary tract during pregnancy was briefly discussed.

6. The technic of amniography has been described, and its field of usefulness as a diagnostic measure has been considered.

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## COMPLICATIONS OF RADIATION TREATMENT IN GYNECOLOGY\*

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THIS paper deals primarily with damage done to the bladder and intestinal tract which makes itself manifest months or years after treatment with radium and/or x-ray for gynecologic diseases.

The treatment of menstrual dysfunction and fibroids requires relatively small doses so few complications arise. An inflammation may occur immediately but it usually clears up in a short time. The infection may be carried in during the operation as believed by Corseaden<sup>1</sup> or it may be present already. It is characterized by pain, temperature and profuse flowing, and examination shows a sensitive uterus with tenderness and sometimes masses on the sides of the pelvis. It is rare in these days of careful diagnosis.

The treatment of cancer of the cervix with radium leads to occasional troublesome after-results. Peritonitis may be due to trauma to, or perforation of, a cancer riddled uterus where infection is already present. Rectal and bladder irritation occur soon after treatment but clear up in a few weeks as a rule. The patients complain of rectal pain and have diarrhea with bloody stools in the former case and tenesmus, frequency and burning in the latter. Treatment to relieve their symptoms is all that is required. Necrosis from overradiation is rare now that the dosage and screening are better understood. Fistulas from the bladder or rectum into the vagina are avoided for the same reason but may occur later in the course of the disease as a result of its progress. Pyometra may occur weeks or months after treatment from contraction and atresia of the cervix but dilatation allowing drainage generally relieves it. Constriction of the ureters may occur soon after treatment

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as a result of swelling, or late when the disease has progressed enough to surround them. A good many cases show a chronic vaginitis which causes adhesions between folds of the vaginal wall even months after the treatment. These are separated by the examining finger easily and cause no trouble. All these complications are well known and are avoided so far as it is possible to do so by accurate diagnosis and regulation of the dose and screening.

We have encountered complications which come on several months after the radium treatment. They are characterized by what may be called devitalization of the tissue accompanied in most cases by an acute inflammation. Therefore they usually happen in cases which have the larger amount of radiation such as cancer rather than in the menstrual dysfunction and fibroid ones.

We have had seven inflammations of the bladder appear in from two months to four years after radium treatment. The patients complain of urinary frequency and burning, accompanied in one to four weeks by tenesmus and pain on micturition. Most of them then have blood in their urine off and on, sometimes at every voiding for two or three weeks. These symptoms continue for about two months in the severe cases and then gradually decrease so that at the end of four months altogether they are well.

The cystoscopic picture in the mild cases consists of a pale center surrounded by an irregular area of edema and redness. In the severe cases there will be a central ulcer up to an inch in diameter, which may be covered with fibrin and later show more or less incrustation with salts. Around this ulcer is a wide area of intense edema with small, very red, velvety patches scattered over it. Occasionally there will be more than one ulceration. As the disease lessens the edema subsides and the ulcer slowly heals over.

This disease can be differentiated from tumor of the bladder because the distress is so much more marked than in tumor and by the great edema and intense inflammation which is not found with new growths. The bleeding from the bladder is terrifying to the patient who knows or suspects that she has been treated for cancer of the cervix. The mental relief which she experiences on being assured that it is due to inflammation and will subside in time is remarkable.

Typical histories are the following:

CASE 1.—C. A., aged forty-eight, married, 4 children. January 21, 1928. A Class A squamous cancer of the cervix was treated with radium applied partly in the cervical canal and partly on the outside, screened with 0.5 mm. of silver and 1 mm. of brass for a dose of 4400 mg. hours.

April 3, 1928. Twelve hundred milligram hours with the same screening.

January 16, 1930. Well except for bladder irritation. Cystoscopy showed a shallow ulcer one inch in diameter in the middle above the interureteric line with edema of the bottom of the bladder. The pyelogram was negative.

She was cystoscoped at intervals and the condition gradually subsided so that it was healed by April 11, 1930.



An unusual case in that nearly four years elapsed between the radium treatment and the bladder ulceration is the following:

CASE 2.—F. S., aged forty-nine, married, 1 child.

February 25, 1923. A Wertheim hysterectomy was done for a Class A adenocarcinoma of the cervix.

October 14, 1925. Thirteen hundred milligram hours of radium were applied in the vagina because of a small indurated area at the top.

April 1, 1929. She began to have bladder irritation followed in two weeks by bleeding from the bladder.

April 17, 1929. Cystoscopy showed an ulceration one inch in diameter between and just above the ureteral orifices.

This gradually healed over so that she was well four months later.

Four of the others occurred in Class A cancers of the cervix treated with from 4800 to 5400 mg. hours of radium screened by 0.5 mm. of silver and 1 mm. of brass in a single dose. The seventh occurred in a diabetic who had a supracervical hysterectomy for cancer of the endometrium because a complete one could not be done on account of obesity and technical difficulties. Three months later she received a vaginal application of 3600 mg. hours of radium as a prophylactic and five months after that her bladder ulcer started. Only one of these patients was treated with x-ray also.

There appears to be little discussion of this complication in the literature. Wille<sup>2</sup> mentions and describes it but offers no explanation. Flaskamp<sup>3</sup> cites Haendly's findings in 127 autopsies. Thirty-six per cent showed bladder disease due to the tumor or radium treatment. In the latter instance it varied from catarrhal inflammation to severe exudation and ulceration always occurring on the posterior wall. Stacy<sup>4</sup> cites a case which showed edema and inflammation appearing four years after a treatment of 1300 mg. hours for cervical cancer and Dean<sup>5</sup> has followed three bladder ulcers coming on fourteen months after treatment.

It is well known that radiation may cause devitalization of tissue but it is interesting that this bladder complication should come on so long after the original treatment, even four years. It seems probable that scar forms, the blood vessels become more or less obliterated, and the bladder wall becomes vulnerable to infection at points where too much radiation has reached it. Then infection and inflammation occur at a later period, going on to ulceration in some cases. The patients do not die, so we have no pathologic description of the lesion. The cystoscopic picture after healing takes place appears to be normal.

It is also interesting that our cases of cancer of the cervix in which this complication occurred were Class A, where there was no thickness of tumor tissue to protect the bladder. It will be noted that the ulceration occurred above the interureteric line in most of them, where the bladder is attached to the cervix.

We think that accurate diagnosis of the condition is important because it may be considered as a continuation of the original disease and more radium or x-ray treatment might be used which would tend to aggravate rather than relieve it. In doubtful ulcers a piece may be removed through the cystoscope for biopsy.

Absolute prevention of this complication would appear to be difficult because of the close association of the bladder and cervix. Measures to lessen its frequency are keeping the bladder empty and packing the vagina with gauze, both of which we always do.

The treatment is expectant and symptomatic. The distress is acute enough at times to require codeine. Locally bladder irrigation and the instillation of an ounce of olive or mineral oil appear to give some relief. We have had no hemorrhage severe enough to cause anxiety.

Stricture of the rectum has occurred after radium treatment in seven of our cancer cases, six of the cervix and one with a vaginal recurrence after complete hysterectomy for adenocarcinoma of the fundus. It forms about two inches above the sphincter ani. These may be divided into two classes.

Five of them were thin strictures just admitting the tip of one finger, easily dilated and the cause of very little trouble. They were noticed in from ten to twelve months after radium treatment with from 2400 to 5400 mg. hours. Two of the patients had experienced bloody diarrhea and rectal tenesmus for a short period after the treatment. One fell in Class A, two in Class B, one in Class C, and the fifth had the recurrence after hysterectomy.

Two cases showed much more fibrosis. A Class A case received 5400 mg. hours of radium and reported five months later with a stricture which was so firm that it had to be incised and dilated under anesthesia. She showed no evidence of cancer seventeen months later so it seems probable that the stricture was inflammatory and not due to cancer. The second patient also fell in Class A. She was treated with 2700 mg. hours in 1922 after which she had rectal tenesmus for several weeks and fourteen months later she received another treatment of 4800 mg. hours for a recurrence. Sixteen months after that she had a colostomy done at another hospital for obstruction in the rectum but, since she died of heart disease with no evidence of a local recurrence nine years after her first treatment, it seems probable that this stricture was inflammatory as a result of the radium treatments rather than due to her disease.

Strictures of the rectum under these circumstances have been noted by several authorities. Jeanneney<sup>6</sup> says that he was the first to call attention to them and that 20 have occurred in 600 cases of cervical cancer which he has treated. Berard and Cryssel<sup>7</sup> found 5 in 200 cases. Jeanneney divides them into two classes which he names intrinsic and extrinsic. The former are like our first 5 cases, easily dilated, thin, soft strictures with a sharp edge which are probably due to a mild, local proctitis caused by radium irritation. The extrinsic ones are firmer, like our last 2 cases and due to inflammation in the perirectal tissues as well as to a proctitis. Berard says that those he has seen are of the latter type because he noted infiltration around the rectum before treatment and believes that there is a cellulitis first which the radiation converts into a sclero-inflammatory perirectal stenosis. It may be that they are due to the replacement of cancer tissue by scar tissue. We think the last is unlikely because when cancer from the cervix encircles the rectum

it does so higher up, in the region of the uterosacral and broad ligaments. This might have been true in our case which required a colostomy but it seems improbable because when the disease is as advanced as that it is unlikely that an apparent cure will result. We believe our cases correspond with Jeanneney's and that the severe, dense stenoses are due to a preceding cellulitis which forms a dense, contracting scar with the added radium irritation.

The treatment is dilatation which is very satisfactory in the intrinsic cases. Berard says that diathermy helps by softening the structures, making dilatation easier and more permanent in the extrinsic ones.

Four distressing complications have occurred higher up in the intestine. Two were strictures of the sigmoid and one a necrosis of the ileum in patients with cancer of the cervix and one an inflammation in the sigmoid adherent to the uterus in a case of menstrual dysfunction.

CASE 3.—A. W., aged fifty-one, widow, 1 child.

December 19, 1927. She was treated for a Class B inverting adenocarcinoma of the cervix with 4800 mg. hours of radium screened with 0.5 mm. of silver and 1 mm. of brass. One month later she complained of pain when her bowels moved.

April 23, 1928. She was having many small movements with much gas and pain. The x-ray examination showed a constriction at the rectosigmoid junction.

May 5, 1928. A laparotomy was done and the sigmoid was found adherent to the back of the uterus with many adhesions between loops of small intestine in the pelvis and marked edema of all the pelvic contents. It would have been necessary to have separated these adhesions with a good chance of doing damage resulting in peritonitis so it was deemed wisest to do a colostomy. She made a good convalescence.

November 30, 1928. The pelvis was negative. An x-ray showed the stricture as before.

April 23, 1929. She began to have some movements through the anus but refused to have anything further done.

January 8, 1930. She had been comfortable, her bowels moving mostly through the anus, some through the colostomy. X-ray showed that there was much less obstruction.

December 4, 1930. Her bowels had moved normally every day but the colostomy had not closed. She refused to have it closed by operation.

January 13, 1931. She began to have severe headaches, which were finally diagnosed as due to a metastasis in the brain, and died soon after. There was no apparent local recurrence.

It is obvious that this complication was due to the sigmoid being adherent to the back of the uterus with damage from the radium as a result. There was no history of an antecedent inflammation or operation to cause the adhesion and no way to diagnose it beforehand. It is interesting that the stricture should have relaxed enough to allow normal bowel movements. The colostomy was done with some difficulty because the patient was fat and the mesentery of the colon was short, in spite of freeing the outer sheet of peritoneum, so a bridge of skin was placed under the loop of bowel to keep it from retracting. That is probably what prevented it from closing entirely when the stricture opened.

CASE 4.—E. D., aged fifty, married, 3 children.

June 4, 1930. She received 4800 mg. hours of radium with the same screening for a Class C inverting squamous carcinoma of the cervix.

December 10, 1930. She had been seen at regular intervals and appeared well. Deep x-ray treatment was started.

June 5, 1931. She had had x-ray treatment as follows:

December 29, 1930. Using 200 K. V., 40 cm. distance  $\frac{1}{4}$  mm. of copper and 1 mm. of aluminum, 5 mm. of current and thirty minutes anteriorly over the lower abdomen through a 20 by 20 cm. Port.

January 6, 1931. Same dosage, thirty minutes, posteriorly.

January 23, 1931. Same dosage, thirty minutes, anteriorly.

February 7, 1931. Same dosage, thirty minutes, posteriorly.

March 20, 1931. Same dosage, thirty minutes, anteriorly.

April 14, 1931. Same dosage, thirty minutes, posteriorly.

She felt well. The local examination was negative.

July 14, 1931. She was operated upon by Dr. H. B. Loder for acute intestinal obstruction which was due to a stricture about five inches above the rectosigmoid junction. This part of the intestine lay in the pelvis behind her cervix. Six inches were resected and an end to end anastomosis done from which she made a good recovery and has been well since.

We were allowed to see the specimen and microscopic slides through the kindness of Dr. S. C. Dalrymple, pathologist at the Newton Hospital, Newton, Massachusetts. The entire thickness of the intestinal wall contained an inflammatory infiltration and there was marked edema of the submucosa with loss of the mucosa in the region of the stricture. The muscle fibers and their nuclei were fairly normal. The blood vessels throughout the section were apparently normal.

In this case the sigmoid was not adherent but it was redundant, so that it lay in the pelvis within the radiation area. An intestinal x-ray before treatment might have shown it, but it would seem too meticulous to do that in every case that we see in order to prevent such a complication. The patient must have had rather an acute inflammatory stage without enough symptoms to trouble her, because she complained of none until the actual obstruction took place, and the pathologic examination showed a well healed scar. It is also possible that the deep x-ray therapy might have played some part by supplying an overdose of radiation; but six months had elapsed since the radium application, and therefore we do not believe it is probable.

CASE 6.—E. H., aged fifty-five, widow, 4 children.

January 2, 1931. She received 4800 mg. hours of radium with the same screening for a Class C carcinoma of the cervix.

January 30, 1931. She had had some bloody diarrhea and rectal tenesmus.

March 13, 1931. She was free of symptoms and the examination was negative.

April 21, 1931. She complained of mild cramplike pain in the region of the pubes. Examination was negative.

April 26, 1931. For forty-eight hours she had had more pain accompanied by vomiting and showed a rigid abdomen, temperature and white count. Operation revealed free fluid and fresh adhesions between coils of intestine in the pelvis but the uterus, tubes, ovaries, and appendix were negative. A loop of ileum ten inches long was lying in the pelvis, its distal end two inches from the cecum. It showed a red, thickened wall with green necrotic areas. Its caliber gradually decreased from both ends towards the middle. There was no twist, old adhesion or other mechanical cause for the condition. This was resected, and an end to end anastomosis done, with an ileostomy six inches above. She died in two days with no distention, nausea or vomiting, apparently from an overwhelming infection.

This loop of small intestine was not adherent but must have remained in the pelvis long enough to have been affected by the radium. The length of the piece and the extent of the devitalization are extraordinary.

The pathologic findings were as follows:

*Macroscopic Examination.*—Specimen consisted of 22 cm. of ileum. The wall was edematous and covered with exudate and fresh adhesions. At the center of the resected gut was a scarred constriction obstructing the lumen of the bowel. The proximal portion of the bowel was somewhat dilated. Section was taken from point of obstruction, also one other section was taken. There was no gross evidence of malignancy.

*Microscopic Examination.*—There was a narrow section of mesentery which contained a marked inflammatory infiltration and normal appearing blood vessels. The serosa was edematous and infiltrated with leucocytes. The muscular layers stained poorly. The muscle bundles could be differentiated but the nuclei had disappeared and the general picture was of a beginning hyaline degeneration. The submucosa was markedly inflamed and edematous. The blood vessels appeared to be normal in number and size. Throughout the section no evidence of obliterating endarteritis was found. The mucosa was lacking, the inner edge consisting of connective tissue covered with exudate.

A section from the end of the piece of bowel showed the normal structure of the wall but there was an inflammatory exudate throughout the layers.

*Diagnosis.*—Acute inflammation, necrosis, hyaline degeneration.

The examination of these two specimens showed no evidence of obliterating endarteritis but did show a good deal of scar and, in one, definite changes in the muscle layers. We feel that endarteritis does not play as important a part as has been supposed in devitalization of tissue by radiation but that the effect is a direct one on the tissue cells. Further since the mucosa was completely destroyed in both of these, epithelial tissue is more vulnerable than others, which is what one would expect from our treatment of cancer.

CASE 7.—M. H., aged forty-eight, married, no children. Bilateral salpingectomy, 1923.

October 7, 1930. She had had profuse menstruation for one year.

Ether examination showed a small fibroid in the left horn of the uterus and the rush diagnosis on the endometrium was endometrial dysplasia. We debated, in view of her previous operation, as to whether to treat her by radium or operation. Since the operation had been seven years before, during which time she had had no symptoms and all examinations had given no sign of tenderness or other abnormality, radium was decided on and 100 mg. screened with 0.5 mm. of silver and 1 mm. of brass was applied in the uterine cavity for twelve hours.

November 28, 1930. For four days she had had a heavy feeling in her pelvis and vomited a few times. This day she complained of a twisting feeling at the navel, radiating all over the abdomen, and vomiting. Examination revealed only tenderness through the pelvis. She remained in the hospital two weeks and was apparently well on leaving.

March 9, 1932. The patient had had no catamenia since her treatment sixteen months before. She complained of having had occasional attacks of pain and discomfort in the rectum. Five days before admission she felt as if something broke in her lower abdomen and began to have fever and discharge. Examination showed induration in the pelvis but no masses.

She was no better at the end of three weeks so operation was decided on. This revealed a loop of sigmoid densely adherent to the back of the fundus of the uterus with an abscess containing two ounces of pus between them. The intestine was otherwise normal. No perforation could be made out and the raw surface was sutured over. A hysterectomy was done because there was so much induration in the parametria. The wound was closed with drainage and she made a good convalescence.

Here again the cause of the complication is evident. The mistake was in treating a patient, who had had a previous pelvic operation, with radium. In order to prevent all such incidents one would have to adhere strictly to the dictum that no

patient who has a history of any previous pelvic inflammation or operation should be treated with radium, regardless of how distant the occurrence was or how free of symptoms the patient has been.

In two of these four cases the intestine was held in the radiation area by adhesions and in the other two the loops must have stayed in the area long enough to have been damaged. We feel that in view of the few cases reported that some of these intestinal complications are not diagnosed. It may be that only a small area is affected in many and that it heals without causing much trouble. Our second case certainly had no symptoms of note before the acute attack. The third one had some pain five days before the emergency operation but there were not enough objective signs to make one suspect that such a serious condition existed.

We can find very little in the American literature about such intestinal complications. Lynch<sup>8</sup> speaks of a patient who "died, two years after treatment, of bowel obstruction of cancerous origin or possibly as a result of radium given when our experience was incomplete." It might well have been one similar to ours. Stacy<sup>4</sup> states that if narrowing of the rectum is noticed before treatment the patient should be kept under observation for two or three weeks after treatment because edema may complete the obstruction and a colostomy be necessary. We have seen no cases like that.

A great deal of experimental work with animals has been done on the effect of x-ray and radium on the gastrointestinal tract. The articles have been collected and reviewed by Desjardins.<sup>9</sup> He concludes that the results of the two kinds of radiation are the same. The immediate effect is an increase in tone and spasticity of the intestinal wall. Then a mucoid and vacuolar degeneration of the epithelium takes place followed by desquamation. A large amount of bloody mucus is found in the bowel. The change may go on to inflammatory infiltration, hemorrhage into the tissue and ulceration. Later there is a formation of connective tissue with stricture and shortening of the intestine. Large numbers of colon bacilli are found in and on the ulcerations but evidence so far is contradictory as to whether or not the bacteria make their way into the blood stream to produce septicemia. Any one application of radiation may not be dangerous but when several are given from various angles they may converge and focus at one place to cause an overdosage with destructive results.

Flaskamp<sup>3</sup> has looked over the world literature up to 1930 and written a complete account of damage done by radium or x-ray in all parts of the body. The section dealing with gynecology cites cases treated with x-ray and/or radium which showed damage to the intestine varying from catarrhal inflammation to necrosis and ulceration. Many of them were due to overdosage. The interesting point, however, is that the damage took place in the more stationary parts of the intestinal tract such as the rectum, sigmoid, and cecum. When small intestine was affected it was usually more or less fixed by adhesions which had formed before the treatment was applied. For instance he cites Eckelt's experience with 21 cases of cancer of the uterus treated by x-ray. Seventeen of them had diarrhea, 8 of these died, and 4 showed ulceration of the intestine where it was adherent beneath the area of treatment. Haendly<sup>3</sup> has done 127 autopsies on patients treated with x-ray and/or radium. In 31 cases (24 per cent) there were evidences of damage to the intestine such as ulceration, stenosis, and necrosis. All parts of the intestinal

tract were affected but in general x-ray hurt the descending colon and radium the rectum more generally. The cecum and lower ileum showed the effects not infrequently and the transverse colon three times. Strauss<sup>3</sup> is inclined to doubt that this complication occurs as often as Haendly states, but he believes it would be noticed oftener if we were on the lookout for it. The symptoms are not regarded seriously enough and the mild cases heal without being diagnosed.

Knowing that such serious complications may occur we are concerned with the prevention of them so far as possible. The dosage of radiation and the screening should be considered most of all. If one is dealing with a Class A cancer of the cervix or cancer in the cervix after supra-cervical hysterectomy the chance of radiating near-by organs is greater than usual and one should vary the treatment accordingly. Now that deep x-ray therapy is used as well as radium we think the chance of overdosage will be greater than it has been and that undoubtedly more of these late complications are going to occur and be diagnosed if we are on the lookout for them. Flaskamp believes that adhesions may be found beforehand by causing pneumoperitoneum and taking an x-ray. If found they may be treated by operation before the radiation is applied. We think that adhesions might well form again immediately. Therefore unless there is a good reason for feeling that there may be some present, such as a history of inflammation or operation, one had better take the slight chance which there is of doing harm in going ahead with radiation. All agree that the intestinal tract should be empty before treatment and most that the bladder should be on constant drainage or frequently emptied during it. No radiation should be given while there is any barium in the intestinal tract because of the danger of necrosis from secondary rays. It might be well to place the patient in the Trendelenburg position during treatment with radium, but it would be rather a strain on her to make it constant for twenty-four hours or more. We hardly think that a lesser degree of elevation would get the small intestine out of the pelvis. She should be told to change her position often as that would tend to move the abdominal contents to some extent. Lying in the Sim's position at intervals would allow the pelvis to empty.

The cases that we have cited were treated at the Free Hospital for Women and in my private practice. The total numbers treated with radiation were as follows:

	F. H. W.	F. A. P.	TOTAL
Cancer of the cervix	382	43	425
Leiomyoma of the uterus	42	28	70
Menstrual dysfunction	422	74	496

The patients at the Free Hospital for Women were treated by Dr. William P. Graves, Dr. George V. Smith, and myself.

We think we may grant that stricture of the rectum and inflammation of the bladder are unavoidable. That is, they will occur occasionally. The case of a fibroid with the sigmoid adherent to the fundus as a result of a previous operation should not have been treated with radium. We

feel that the other three intestinal complications were unavoidable accidents bound to happen when one is dealing with large doses of radium and x-ray in the treatment of cancer.

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## ✓ TWELVE YEARS' EXPERIENCE WITH (UTEROTUBAL) INSUFFLATION; DIAGNOSTIC AND THERAPEUTIC\*

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## INTRODUCTION

THE specific object for which uterotubal insufflation was originally devised was to replace exploratory laparotomy in the diagnosis of the tubal cause of sterility. It was felt that once the integrity of the female genital tract could be demonstrated without resorting to an operative procedure, we would be able to avoid doing needless operations upon the uterus, especially upon the cervix. We should, thus, be able to treat sterility more intelligently.

Intensive study of human sterility during the last twelve years has brought out many causative factors which heretofore had not been adequately estimated. The last decade has witnessed a steadily growing interest in the functional (inner secretory), chemical, and serologic aspects of human reproduction. In the light of this newer work the patient's constitution has been reinterpreted.

After a little more than twelve years' experience with uterotubal insufflation it has become possible to estimate the importance of non-patent tubes in any sterile mating. The purpose of this paper is to present the findings in a fairly large series of sterile women especially from the viewpoint of the tubal factor.

Obviously, the determination of the tubal status by no means exhausts the investigation of sterility. Due consideration was given to all other important etiologic factors. But it was necessary to establish as fully as possible the diagnostic value of uterotubal insufflation. Only in this way could it properly be compared to other methods.

A by-product of the investigation of the diagnostic aspects of uterotubal insufflation was its therapeutic value. The determination of the therapeutic value remains subject to greater differences of opinion and interpretation than is the diagnostic value of insufflation.

Another phase of the work has been the resumption of the use of

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opaque solutions which Cary<sup>3</sup> and I<sup>4</sup> employed independently in 1913 and 1914 but which were abandoned because of certain disadvantages. The earlier solutions, collargol, sodium bromide, sodium iodide, and thorium have been replaced by lipiodol and other iodized oils, which are less irritant and more radiopaque.

Opaque solutions with the aid of x-rays had been proposed for the localization of tubal obstructions, but increasing experience with uterotubal insufflation has made such examinations unnecessary except in a few special instances. During the period of investigation lipiodol has served the purpose of checking the findings and interpretations in certain details, and more particularly in the study of tubal sphincters. In my work lipiodol is now reserved for a relatively small group of cases where the fallopian tubes prove to be closed by the gas method or to be the seat of high grade obliterating tubal strictures.

Time does not permit full reference to an extensive literature on tubal insufflation with numerous excellent reports by workers here and abroad, to whom a large measure of the progress that has been made is due. These reports are included in a monograph now in preparation which, it is hoped, will be forthcoming in the near future.

#### INDICATIONS

Sellheim,<sup>21</sup> in writing on seven years of tubal insufflation, considers "the examination of the patency of the tubes just as important as the determination of the accessibility and functional fitness of the vagina and uterus which are always investigated. The procedure of the examination of the tubal functions has been made so free from danger that a thorough gynecologic examination should almost be considered incomplete if an investigation of the functional fitness of the tubes is omitted. The physician should be interested to get a clear picture of this vital question."

The cardinal indication for uterotubal insufflation is to determine the patency of the fallopian tubes. The method has been found useful:

1. In deciding upon the advisability of an operation to relieve sterility.
2. As a postoperative measure to test and maintain the patency of the newly formed stoma (salpingostomy, salpingolysis, and tubal reimplantations into the uterus).
3. To check the results of a tubal sterilization operation.
4. To determine the secondary effect upon the tubes of induced abortions, uterine retrodisplacements and appendicitis.
5. To determine the condition of a residual tube after tubal pregnancy.
6. To study the physiology of the tubes, especially in such conditions as functional amenorrhea during the reproductive period, during the menopause and following x-ray castration.
7. To determine the tubal status before prescribing contraceptive measures in suitable cases.
8. As treatment for dysmenorrhea.
9. To produce a pneumoperitoneum as an aid in the diagnosis of obscure abdominal lesions.

10. Its application has been extended by veterinarians to valuable breeding animals where sterility was traceable to abnormalities of tubal patency.

*Exceptional Indications.*—A few patients whose husbands have been found azoospermic have nevertheless wanted to know the condition of their tubes. A few patients who were married only a short time also sought aid early because a sterile sister may have warned them against treatment too long delayed. Advanced age or the desire to settle an estate have been other reasons.

*Contraindications.*—Increasing experience has justified these conclusions as to when the test is contraindicated. They are:

1. *Inflammations of the Genital Tract.*—The test should not be done in the presence of acute or subacute inflammations, whether they are in the nature of an endocervicitis, colpitis, or salpingitis. In order to rule out the presence of inflammatory processes, white blood counts, vaginal and cervical smears, and sedimentation tests are employed. As the indication for the test is never imperative any questionable conditions should be observed over an adequate period, so that the insufflation will be performed at the most suitable time.

2. *Menstruation and the Premenstrual Phase.*—The theoretical possibility of endometrial dislocation and embolism formation precludes the use of the test at these cyclical phases. Because of the further theoretical possibility that insufflation might interfere with an already existing pregnancy, it is not advisable to practice it in the premenstrual period. Furthermore, the mucosal congestion, swelling and spasm incidental to menstruation and the premenstrual period may make higher pressures necessary to permit the gas to pass the uterotubal junction and so lead to false conclusions.

3. *Abnormal Bleeding From the Genital Tract.*—Experimental and clinical observations have shown that this condition may favor emboli. Theoretically too, infections are more prone to occur at this time.

4. *Pregnancy.*—Except for its scientific value in isolated cases, there would seem to be no point in performing a test for tubal patency when pregnancy exists. However, should the test be performed accidentally during this period, it is not likely that any harm will result. Thus, Peterson and Cron<sup>13</sup> insufflated two patients during early pregnancy through mistaken diagnosis. Both patients were delivered of normal children. Titus<sup>22</sup> and Moench<sup>24</sup> have had similar experiences. No untoward results were encountered in ten patients of my series who were insufflated during pregnancy.

5. *Severe Constitutional Diseases.*—As severe constitutional diseases such as cardiovascular disease, severe diabetes and active pulmonary tuberculosis contraindicate pregnancy, tubal insufflation is out of place.

6. *Neurosis.*—Patients with a frankly neuropathic disposition do not stand the test well and in such cases I have not recommended its use.

#### COMPLICATIONS

In the present series of 3600 insufflations there were no serious complications. Twenty-seven patients felt momentarily faint. In 7 instances the patient fainted and was quickly restored. Darkness during the fluoroscopic examination appears to be an exciting cause. To avoid syncopal attacks, patients have been questioned as to whether they faint easily. Their answer has proved useful in avoiding this not very serious complication. Two patients in whom an epileptic tendency had been overlooked had an attack brought on by the test.

Staining during the performance of the test or shortly after is not infrequent. This is of no special importance. In my earlier cases, when the method was tried out under varying conditions in order to determine its safety, there were three instances of mild pelvic irritation, which quickly subsided with rest in bed. Scrupulous attention to indications and contraindications as set forth above, have prevented untoward accidents and sequelae in later experience and the last 2800 insufflations have been entirely without unpleasant symptoms.

#### TIME OF ELECTION FOR INSUFFLATION

The postmenstrual phase, from the fourth to the seventh day following the cessation of the last regular period, has been found the interval of choice for performing insufflations. Interference with a possible pregnancy is thus avoided.

#### OFFICE PROCEDURE

Insufflation has been carried out exclusively as office routine. The patients were always able to return home soon afterward and to perform their usual duties. No preparation, save possibly a good night's rest, is required in the majority of cases. An apprehensive patient may need an anodyne but this is rare. In no case was it necessary to resort to an anesthetic for the test.

*Apparatus.*—A very decided improvement has been made in the apparatus used for the insufflation. The present apparatus combines quantimetric, manometric and kymographic parts, and assures a uniform pressure rate of flow within given limits, i. e., twenty to thirty seconds to inject 30 c.c. of carbon dioxide. This is of the greatest importance. Somewhat slower rates are also serviceable but a more rapid flow is not to be recommended. If the gas is introduced too rapidly, the pressure will be unduly high and lead to wrong interpretations. This is often the case when the syringe and bulb types of apparatus are employed.

With such "simplified" apparatus, important points such as the degree of patency, the presence of peritubal adhesions and uterotubal spasm are missed. By the addition of the kymograph in 1925, a number of physiologic and pathologic data have been obtained that will be briefly detailed later. As Mikulicz-Radecki<sup>10</sup> has said, we are just beginning to realize its scientific value. By the exclusive use of carbon dioxide gas, which is rapidly absorbed, discomfort and shoulder pains have been reduced to a minimum. Large quantities of carbon dioxide gas, necessary to produce a subphrenic pneumoperitoneum for pelvic diagnosis, are rapidly absorbed.

*Sounding the Uterus.*—The uterine sound has not been used as a routine. As a rule, palpation of the uterus and inspection of the cervix enable us to judge the length of the uterine cavity, its direction and whether or not the cannula may be easily introduced.

If a uterine sound is used just before insufflation is performed, it should be handled with the greatest gentleness as it may be followed by bleeding. The uterine cannula should be introduced to just beyond the internal os engaging the external os by its rubber acorn, to avoid pushing the metallic tip into the myometrium or possibly perforating the uterus. These are accidents which happen rarely but should be borne in mind. True cervical stenosis has been discovered in a certain number of instances by the inability to introduce the cannula into the uterine cavity. This condition is not without etiologic importance and must be corrected before the condition of the tubes is tested.

*Findings With the Aid of the Kymograph.*—The kymograph enables us to obtain a permanent and accurate record of the tubal status. The characteristic findings of normal patency, of nonpatency and spasm have been described elsewhere; they will not be detailed here. The findings in the case of strictures and peritubal adhesions deserve special consideration as they point to the difference between insufflation and lipiodol injection.

*Tubal Strictures and Peritubal Adhesions.*—When the tubes are strictured, the pressure rises in a curve, the descent is more gradual and there is apt to be complete absence of typical oscillations. The initial rise of pressure is usually well over 100 mm. Hg, more often between 150 and 200 mm. Hg. In the relatively mild strictures due to circumscribed adhesions there may be noted atypical oscillations which are very shallow and arrhythmic. When the tubes are bound down lightly as by filmy adhesions which do not distort, there may be only the slightest variation from the normal.

If the tubes are bound down by firm adhesions on all sides so that their motion is impaired, the rhythmic contractions are not seen although the pressure levels may not not exceed the normal. Experimental work has shown that isthmic stenosis blocks tubal peristalsis and interferes with rhythmic contractions more markedly than ampullary or fimbrial stenosis.

Occasionally, one encounters a case where the fluctuations are slight and the gas is also regurgitated. If the gas has succeeded in entering the peritoneal cavity, a rise of pressure will be produced when the patient bears down, coughs or sneezes. When the kymograph is not available, it is possible to plot a curve by noting the rise and drop of the manometer. The curve thus charted is of aid in distinguishing between normal patency, peritubal adhesions and uterotubal spasm. When hysterosalpingography alone is employed it is not possible to diagnose these conditions, except in rare instances.

*Vaginal Palpation.*—Immediately after insufflation vaginal palpation may demonstrate a distended tube which will be empty a few minutes later. In the absence of regurgitation this would point to the presence of spasm or some stricture at the fimbriated end which has been overcome. Occasionally, one will palpate a hydrosalpinx which may hold as much as 150 c.c. of gas. Hence, if the amount of gas injected is comparatively small as when the syringe and bulb types of apparatus are used, one may be led to false conclusions. Occasionally, emphysema is encountered which disappears without causing further trouble.

*Shoulder Pains.*—Shoulder pains occur in the presence of gas under the diaphragm. The amount of gas allowed to enter the peritoneal cavity and to rise to the subphrenic space, in relation to the particular patient's weight and abdominal and chest measurements determines the intensity of the shoulder pains. A thin individual whose waistline is narrow requires less gas for the production of a well marked subphrenic pneumoperitoneum than an obese person. In general when a fluoroscope is not at hand at least 100 c.c. of carbon dioxide gas should be used. The patient should rise as soon as possible to note whether shoulder pains occur. The knee chest or recumbent position relieves them at once. Prolonged shoulder pains are usually due to failure to displace the air in the rubber tubing by carbon dioxide gas before introducing the cannula into the uterus.

*The Fluoroscope.*—The fluoroscope is an important objective aid in the diagnosis of tubal patency. The depth of the subphrenic pneumoperitoneum, other things being equal, is a practical guide as to the type of patency. In strictured tubes the gas bubbles, forced through the narrow apertures, are smaller and some of the gas is lost by regurgitation.

In a few instances, part or all of the gas is caught by adhesions in the pelvis surrounding the tubes, or it is prevented from rising to the diaphragm by subphrenic

adhesions. In such an event, shoulder pains are absent. Delayed shoulder pains are due to the gas being entrapped in the pelvis and gradually escaping upward along the abdominal gutters to the diaphragm.

In obese individuals, occasionally, fluoroscopy will be negative although the kymograph has already given proof that tubal patency exists.

Subphrenic pneumoperitoneum may appear on either side irrespective of the side of patency. The gastric vesicle may sometimes be misleading. If there is any doubt the patient should be instructed to lie on the left side; pressure is then exerted over the right chest after which the gas is seen under the right diaphragm. Here it is unmistakable. The pneumoperitoneum is apt to persist longer on the right than on the left side. The contractions of the stomach appear to further the escape and wider distribution of the gas.

*Localization of the Site of Tubal Obstructions.*—In the presence of normal patency patients do not feel the slightest pain referable to the tubes themselves. They may complain of a sense of discomfort in the suprasymphyseal area, referable to the uterus which is momentarily distended, and lasting for the brief period before the gas passes through the uterotubal junction. Complaint of slight discomfort on one or the other side of the abdomen is only occasionally met in normal tubes.

In the presence of tubal stenosis, peritubal adhesions and nonpatency there is, as a rule, some pain referable to the tube affected. Pain reactions have been found to begin at 120 to 150 mm. Hg in closed or strictured tubes. Where adhesions exist, their stretching may cause pain at a much lower level. The obstruction in some cases is bilateral, in some unilateral. The location is symmetrical or asymmetrical.

Distention pain which does not radiate and is referred to the mid-line in the suprasymphyseal area points to an obstruction at the uterotubal junctions. Pain of the same character but also located somewhat laterally indicates isthmical obstruction. Pain radiating well out to the sides indicates an obstruction at the ampulla. The nearer to the fimbriae the site of obstruction is situated, the more marked is the pain. The pain may radiate to the lumbar region and sometimes down one thigh or the other. This pain reaction is stressed because of its diagnostic significance, but it is tolerated by practically all patients and lasts only for the brief time required for the insufflation. It must not be forgotten that pain is also incidental to lipiodol injection. From observation in my cases, this sensory reaction is more prolonged when lipiodol is used than during insufflation.

When only one tube is normal, the kymograph registers normal patency, but abdominal auscultation and careful notation of the pain reaction will point to the side of the obstructed tube. Auscultation, however, is not absolutely diagnostic as the sound elicited may be transmitted to the side of the nonpatent tube. The purring, hissing or gurgling sound is, as a rule, more audible on the side of the patent tube.

In normal patency the tubal bruit is found to be intermittent, the silent phase corresponding to the rise in pressure and the contraction phase of the tube. In adherent and strictured tubes, this bruit is more constant, the typical intermissions being absent. In retroflexed uteri when the tubes are prolapsed, it may be impossible to distinguish between the tubes because of the close proximity of their fimbriated ends. Another source of confusion may be the presence of a hydrosalpinx, having a capacity of 150 c.c. or more. Upon auscultation the sound of the gas passing into such a tube must not be mistaken for bubbles percolating through the fimbriated end. In such cases and others the kymograph and the fluoroscope are of particular help in establishing an accurate diagnosis. And so likewise is vaginal palpation before and after insufflation.

The data obtained at insufflation were analyzed and checked by: (1) experiments upon surviving extirpated uteri and tubes and upon these

organs removed from the sow, (2) laparotomy observations, and (3) findings after lipiodol injections. The experimental side has recently been gone into in detail and will be published in the near future.

#### LAPAROTOMY FINDINGS

Invaluable information concerning the interpretation of insufflation findings was derived from 186 cases in which the tubes could be studied in relation to laparotomy findings. In the patients not operated upon by myself, data concerning the operative findings were obtained from reliable sources.

1. Normal tubal patency	was checked by laparotomy in 28 cases.
2. Tubal nonpatency	was checked by laparotomy in 20 cases.
3. Peritubal adhesions	was checked by laparotomy in 22 cases.
4. Tubal stenosis	was checked by laparotomy in 12 cases.
5. Status of a residual tube	was checked by laparotomy in 72 cases.
6. Insufflation findings before and after tubal operations	was checked by laparotomy in 25 cases.
7. Status after tubal ligation	was checked by laparotomy in 7 cases.

#### LIPIODOL EXAMINATIONS

In the present series, uterotubal lipiodol examinations were performed in 132 cases as a further check upon insufflation. In 92 cases the insufflation findings of nonpatency, and in 23 cases the diagnosis of high grade strictures, were confirmed. In 9 cases of tubal obstruction the lipiodol succeeded in passing the fimbriated end at higher pressures than were employed at insufflation. On the other hand, in 8 cases the tubes were patent to insufflation but not to lipiodol. Intrauterine lipiodol injections have been limited in my work to those cases where insufflation has shown the presence of closed tubes or high grade strictures.

In the 132 cases examined by lipiodol, 6 patients had a peritoneal inflammation of mild grade. Three others developed pelvic abscesses requiring operative intervention. In contrast to these complications not one accident was encountered in this series of 132 patients as a result of the insufflation, although the test was performed at least twice in 123 and as many as seven times in some patients of this control group.

#### ANALYSIS OF THE TUBAL STATUS

In 81 patients of the total series, a diagnosis of the tubal status was not made because only one test was done and the data obtained were

TABLE I. TUBAL STATUS OF 2192 STERILITY PATIENTS

	NUMBER OF PATIENTS	PERCENTAGE
Normal patency	947	43.20
Nonpatency	572	26.10
Spasm-normal patency	103	4.70
Peritubal adhesions and tubal strictures	570	26.00
Total	2192	100.00

insufficient. Failure to diagnose was due largely to stenosis of the cervical canal; the cannula in these cases, had not succeeded in completely passing the internal cervical os. In some apprehensive patients the test could not be completed. A few out-of-town patients did not return for further study.

#### PROGNOSTIC IMPORTANCE OF UTEROTUBAL INSUFFLATION

In general, all other factors being equal, patients with normal tubal patency and function may be offered a good prognosis. The prognosis should be guarded in patients with stenosed and adherent tubes. Repeated insufflations not infrequently improve the status and accomplish a cure. When the tubes are repeatedly found obstructed at 200 mm. Hg, the prognosis must remain poor unless further improvement takes place as a result of insufflation.

#### ANALYSIS OF THE TUBAL STATUS IN RELATION TO SPECIAL FACTORS

Analysis was made of the tubal status following induced abortions and appendicitis, and of the residual tube following extrauterine pregnancy. Further analysis was also made of the condition of the tubes in association with uterine fibroids and uterine retrodisplacements.

TABLE II. TUBAL STATUS IN RELATION TO SPECIAL FACTORS

	NORMAL PATENCY		PARTIAL OBSTRUCTION		NONPATENCY	
		PER CENT		PER CENT		PER CENT
Induced abortions	72 cases	39.78	13 cases	7.18	96 cases	53.04
Appendicitis	121 cases	39.54	98 cases	32.03	87 cases	28.43
Fibroids	37 cases	42.04	34 cases	38.64	17 cases	19.32
Residual tube (tubal pregnancy)	13 cases	18.06	28 cases	38.88	31 cases	43.06
Retroflexions	94 cases	34.82	86 cases	31.85	90 cases	33.33

#### THE INFLUENCE OF OVARIAN HORMONAL FUNCTION ON THE FALLOPIAN TUBES

Clinical tubal insufflation was employed in order to determine a possible secondary effect upon tubal contractions during different phases of the ovarian cycle. Fifty-nine women were insufflated on the tenth to the sixteenth day of the cycle, counting from the first day of the preceding menses. The type of contractions was then compared to that in an equal number of patients who were insufflated from the seventh to the tenth day of the cycle and an equal number from the sixteenth to the twenty-eighth day of the cycle.

The uterotubal tonicity, as measured by the initial rise of pressure at which the gas passes the uterine junction into the tubes, was decidedly higher in the group insufflated on the tenth to the sixteenth day of the cycle, and the rate and depth of tubal contractions were also greater.

In 120 cases of amenorrhea there was a striking decrease in uterotubal tonicity, in the rate of the contractions and in their amplitude. These patients also exhibited a contraction fatigability manifested by a decrease in the rate and depth after a minute or two. In 5 cases of ovarian hypofunction, the tubes were insufflated before and after stimulating doses of x-ray and radium. After such "ovarian stimulation" there was an increase in the contraction rate in all five and an increase in the amplitude of the contractions in four.

Seven patients were insufflated during the menopause. In three instances the initial rise of pressure was below 50 mm. Hg. There were no tubal contractions in three instances; in four the contractions were infrequent and rarely reached above 5 mm. Hg.

The effect of castrating doses of x-ray irradiation of the ovaries, in relation to tubal function, was studied in 33 women. These were patients from the gynecologic service at Mount Sinai Hospital who were treated by the x-ray department in order to produce a therapeutic abortion for various vital indications. Twenty-two or 66.6 per cent had initial pressure rises under 50 mm. Hg, as compared to 13 per cent in untreated patients with normal periods. The contraction rate was not decreased for the first minute or two, after which however, the tubes become fatigued, exhibiting infrequent and shallow fluctuations.

#### THERAPEUTIC VALUE OF INSUFFLATION IN STERILITY

The therapeutic value of insufflation has been demonstrated in two ways: (1) by the improved status of the tubes as seen at once during the first application, or in subsequent tests; (2) by pregnancy following closely upon insufflation.

In the present series, 44 patients with peritubal adhesions showed improvement at a subsequent test while 43 others eventually showed normal patency and function. Sixty-three patients with tubal stenosis and 22 with uterotubal spasm showed improvement after repeated insufflations. The effect of repeated insufflations was most striking, however, in 116 cases which showed varying degrees of tubal patency after a negative initial test. In 41 instances improvement was noted on the kymograph during a first examination, the insufflation being prolonged for several minutes. Repeated tests were usually done when the tubes were found obstructed. One patient had twelve tests.

The therapeutic effect of the method is best judged by the pregnancies that have occurred promptly or very soon after insufflation, particularly in patients who were sterile for more than five years and in whom tubal patency and function were found to be impaired.

There have been 764 pregnancies collected from the literature and personal communications, all of which have been attributed directly to insufflation.\* Undoubtedly, a greater number have not been reported.

\*An analysis of statistical reports of larger and smaller series, kindly forwarded to me, will be given in the future.



Among those who have reported pregnancies for which insufflation may be credited are: Anspach,<sup>1</sup> 18 cases; Campbell,<sup>2</sup> 14 cases; Ferguson<sup>4</sup> and Graff,<sup>5</sup> 38 cases each; Greenhill,<sup>6</sup> 52 cases; Mandelstamm,<sup>7</sup> 61 cases; Mayer,<sup>8</sup> 98 cases; Meaker,<sup>9</sup> 30 cases; Mombach,<sup>12</sup> 16 cases.

In my own series 398 women or 17.50 per cent of those who were insufflated for sterility became gravid. If we consider only the 1620 cases in which some degree of patency was demonstrated, the percentage is 24.57 per cent.

TABLE III. INCIDENCE OF PREGNANCY RELATIVE TO TUBAL STATUS

	TOTAL CASES	NUMBER PREGNANT	PERCENTAGE
Normal patency	947	254	26.82
Spasm-normal patency	103	21	20.38
Strictered and adherent tubes	570	123	21.58

The therapeutic results were particularly noteworthy in the 570 cases of sterility in which there was some organic interference in tubal patency, i. e., adhesions or strictures. One hundred and twenty-three or 21.58 per cent of this group became gravid.

At least one out of five patients coming for the relief of sterility, and whose tubes were not permanently sealed, became pregnant after insufflation. It may be noted in this connection that no systematic questionnaire had been sent out to these patients, the reports being voluntary. It is likely that the percentage of pregnancies would be higher if all data were available.

There were 269 patients or 67.59 per cent of the successful cases who became gravid during the first six months after the test. There were 168 or 42.21 per cent of the gravidities that took place within two months of the test. There were 111 or 27.89 per cent that became gravid within a month after the test. This short interval would appear to be a fair criterion of the therapeutic effect of insufflation. The fact that 53 patients became gravid two years or longer after the test should caution us against making a poor prognosis when pregnancy does not follow at once.

Of the 244 primary cases of sterility who became gravid there were 54 or 22.13 per cent who had been sterile for over five years before they were treated by insufflation. There were 68 women or 44.15 per cent of the 154 secondary sterility cases who had found themselves unable to conceive for five years or longer after their last pregnancy. Twelve patients had been sterile for more than fifteen years.

Insufflation was the only treatment employed in 247 of the 398 patients who became pregnant (62.06 per cent). The therapeutic measures besides insufflation that were employed in the remaining 149 cases are too varied to take up here.

The manner in which uterotubal insufflation exerts a therapeutic influence has been discussed elsewhere. Here it is well to recall the criteria by which to estimate the responsibility of this treatment in any given case:

1. The age of the woman should be thirty years or over.
2. Pregnancy must follow within a month or at least two months after tubal insufflation.
3. The length of marriage should be three years or longer.
4. The patient must not be treated by any other measure than by tubal insufflation.
5. The insufflation should be done within the first two weeks of a last regular period or in the preovulation phase.
6. Patients must not have taken contraceptive precautions for at least one year prior to insufflation.

Repeated insufflation accompanied by successively lower pressures and other signs of normal patency may be assumed to be therapeutic. If pregnancy takes place after such treatment it may be attributed to the insufflation.

These criteria are more or less arbitrary. But obviously, there must be some standards by which to gauge and evaluate the results of this and other measures which are adopted in the treatment of sterility and to calculate their comparative values.

Experience of most workers here and abroad with uterotubal insufflation has established the ratio between open and closed tubes. This varies between definite limits and depends upon the particular group of patients studied and upon the application of the method. In general, the difference in the reports of most authors is not great. In 26.10 per cent of my series the tubes have been found to be occluded, and in 26 per cent they were partially obstructed. These figures require no comment. They should help to evaluate the etiologic factors in sterility without minimizing or exaggerating their relative importance.

#### TREATMENT OF DYSMENORRHEA BY INSUFFLATION

The therapeutic effect of insufflation on dysmenorrhea, first reported by Peterson and Cron,<sup>13</sup> was studied in 57 cases of sterility. Twenty patients were cured of their dysmenorrhea and 18 were improved for as long a time as they were under observation; 19 patients were unimproved. Eleven patients reported relief for a year or longer, one for seven years.

#### SUMMARY AND CONCLUSIONS

1. Insufflation was employed as a diagnostic and therapeutic measure in 2273 cases of sterility, and in 154 additional cases for other indications. There were 3600 insufflations performed in all.
2. Genital inflammations, menstruation and the premenstrual phase, abnormal bleeding from the genital tract, pregnancy, and severe constitutional diseases contraindicate the test.
3. There were no serious sequelae in the 3600 insufflations herein considered.

4. The postmenstrual phase, from the fourth to the seventh day following the cessation of the menses is the most favorable time to insufflate the tubes.

5. The use of the uniform pressure rate flow of gas within definite time limits is essential for safety. Carbon dioxide is preferred because of its rapid resorption.

6. With the aid of the kymograph the presence of tubal patency, of nonpatency, tubal stenosis, peritubal adhesions and uterotubal spasm can be determined.

7. In the vast majority of cases it is possible to locate the site of obstruction. The decision for or against operation to open the tubes is thus rendered possible. In this respect, abdominal auscultation and careful notation of the sensory reactions during examinations are important.

8. The interpretation of insufflation results has been confirmed by experimental methods and by the findings at 186 laparotomies and 132 lipiodol examinations. In this connection it is worthy of note that although no complications arose in the 132 cases from insufflation, there were sequelae following the lipiodol in 9 cases. Three of these were pelvic abscesses requiring surgical intervention.

9. Of the 2192 sterility patients in whom the status of the tubes was satisfactorily determined, 947 or 43.2 per cent had normal patency. There were 1245 patients or 56.8 per cent who had various degrees of tubal obstruction. There were 572 patients or 26.1 per cent of the total series who had complete tubal obstructions. These figures may form a basis of comparison with other etiologic factors in sterility, and eventually help to evaluate their relative importance.

10. The incidence of tubal obstructions following induced abortions was 60.22 per cent; following appendicitis, 60.46 per cent. Obstructions were found to associate fibroids in 57.96 per cent and retroflexions in 65.18 per cent. The residual tube following an extrauterine pregnancy was found obstructed in 81.94 per cent.

11. The contraction rate, amplitude and uterotubal tonicity are increased in patients insufflated during the 10th to the 16th day of the menstrual cycle, i. e., at the time when we would expect ovulation to occur.

12. The contraction rate, amplitude, and uterotubal tonicity are decreased in functional amenorrhea of young women, during the menopause and after x-ray castration.

13. Tubal insufflation appears to have a definite therapeutic value in sterility. This is demonstrated by actual improvement in tubal patency and function during prolonged or repeated insufflation as recorded on the kymograph, and by pregnancy which follows soon afterward.

Of the 398 patients who became gravid after insufflation, 123 or 21.58 per cent had peritubal adhesions or stenosed tubes. In this respect insufflation may be considered as a nonoperative method of salpingolysis.

There were 67.59 per cent of the gravidities that took place during the first six months after insufflation, 42.21 per cent within two months, and 27.89 per cent within a month.

Of the 244 primary cases of sterility who became pregnant, 22.13 per cent had been married for over five years before they were treated by insufflation. Of the 154 secondary cases of sterility who had found themselves unable to conceive for five years or longer after their last pregnancy 44.15 per cent also became pregnant after treatment. Pregnancy followed treatment in 12 women who were sterile more than fifteen years.

Insufflation was the only treatment employed in 247 of the 398 cases that became pregnant (62.06 per cent).

14. Improvement of dysmenorrhea followed insufflation in 66.6 per cent of 57 patients.

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# THE SELECTION OF APPROPRIATE OPERATION FOR THE CURE OF PROLAPSE\*

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MY INTEREST in the treatment of vaginal and uterine prolapse dates back more than twenty-five years. From 1914 to 1917 I studied the anatomy in detail and in 1917 described a technic applicable particularly to cystocele.<sup>1</sup> In 1923 an even more detailed publication of the operative technic, based on the anatomy of the parts, was published.<sup>2</sup> Since then my interest has continued unabated and I have tried out a number of operations applicable to certain special cases. In the main, however, my interest has centered in perfecting a technic applicable to the average case.

Injuries to the birth canal may be grouped under three headings which are noted alone or in combination. The main types are descent of the anterior (cystocele) and posterior (high and low rectocele) vaginal walls, and descensus of the uterus. These occur in various degrees of severity and may be complicated in the case of cystocele, with incontinence, and in the case of both cystocele and descensus, with kidney damage. No two cases are alike. Almost always these conditions appear in parous women. Only exceptionally are they found in the nullipara and then most frequently as a sequel to the nerve injuries accompanying spina bifida.

In describing the anatomy previously, I have followed the accepted scholastic descriptions which unnecessarily complicate the subject.<sup>1, 2</sup> From the viewpoint of the operator, the position and motility of the cervix, and to a large degree, dependent on this, the tenseness and intactness anteriorly of the pubocervical tissues, and posteriorly of the firmness of the rectovaginal planes as well as the depth of the Douglas culdesac, are the main features to be considered. This does not signify that the position of the fundus is entirely negligible. The levator ani and its fasciae appear to play a minor rôle in repair although the intactness of this diaphragm safeguards greatly against the development of descensus. In repair, however, the levator and its fasciae serve merely as accessory aids and are utilized in fixing the midportion of the rectum and in building up a strong and efficient perineum.

The nature of the injury plays the leading, but not the exclusive rôle, in determining the anatomic lesion and its extent. The site of the injury, its degree, its type, whether due to stretching of the structures or to submucous or open tears, each play their part.

More and more attention has been focused, as the years have passed, upon the constitution of the patient, including the general body con-

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figuration, the robustness or its opposite, the asthenia, the presence or absence of enteroptosis, the strength or weakness of the fasciae, and the complication of obesity. In other words, the constitution or make-up of the patient appears to play a not inconsiderable rôle, which if I should venture to put it upon a percentage basis, would influence at least 25 per cent in favor of or against a successful result.

Moreover, individually varying factors, such as age handicap, poor surroundings and poor living conditions, somatic complications especially cardiorenal diseases, pulmonary troubles, particularly bronchitis and emphysema, markedly influence the outcome and play an important part in the proper selection of operative procedures. Social conditions are of utmost importance. The results in my private practice, composed largely of women in favorable surroundings and able to take good pre- and postoperative care of themselves, are immeasurably better than in the ward cases, consisting of a group of women who soon, postoperatively, must return to hard and continuous work.

An unusually careful follow-up, undertaken by Drs. Howard Lindeman and Max Mayer, just completed, has given me much additional information. This follow-up was performed with a scrupulous exactness, with every effort to minimize success and accentuate failure. Of 480 cases available, only 414 were accessible to this minute scrutiny. Of these, 183 have as yet been followed up for less than a year (three months to twelve months). There have been 231 cases followed up from eighteen months to two years or more. From my point of view the results are extremely discouraging.

Good	46%	} Satisfactory	66%
Adequate	20%		
Inadequate		} Unsatisfactory	34%
Poor (including hernia)			
Improved	82%		

Among the poor plastic results are included 21 patients who developed ventral, incisional hernia after ventrofixation. In this group of 21, the vaginal repair was good in 16. Hernia developed in 21 of 200 ventrofixations (10.5 per cent).

The occurrence of hernia after ventrofixation appears to be directly proportional to the amount of drag exerted by the uterus, and exceeds immeasurably the number of hernias found in other laparotomies, 0.8 per cent.

Another noteworthy observation was the fact that incontinence in the absence of cystocele, rectocele, or prolapse (5 cases) was not cured in any. This is in sharp contrast to the general run of incontinence cases of which 62 per cent were cured by operation.

The operations performed over many years for the cure of cystocele,

rectocele, and prolapse consisted of vaginal plastic repair and ventrofixation.

Anterior colporrhaphy was done according to the technic described by me in 1917,<sup>1</sup> in which the bladder is fully mobilized and the pubocervical tissues united in the midline, their cervical base being attached higher up on the anterior surface of the uterus.

The operation for rectocele consisted, in low rectocele, in the exposure and freeing of the rectum, exposure of the fasciae covering the levators

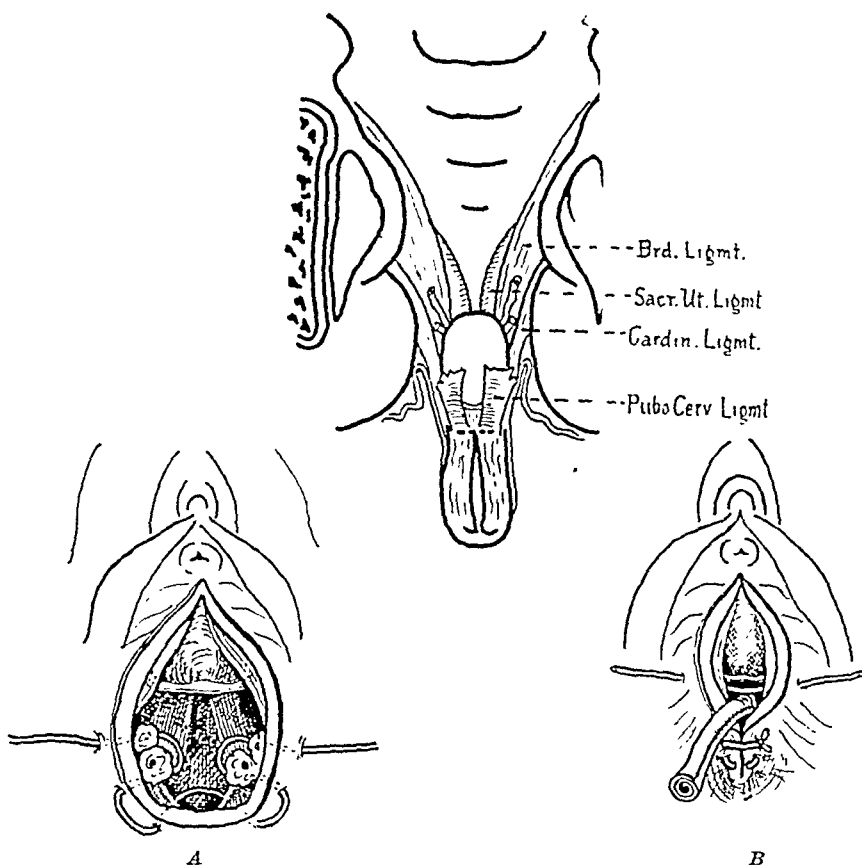


Fig. 1.—Vaginal hysterectomy for prolapse. Top center, schematic transverse section of pelvis showing uterus pulled down with elongation of all ligamentous and cellular structures. Transverse dotted line at internal os. A, uterus removed. Parametria ligated. Suture shown before tying, including cardinal ligaments, sacrouterine ligaments and posterior vaginal fornix. B, suture tied. Intraperitoneal rubber tissue drain. First anterior suture passed.

which, without baring the muscles, were brought together in the median line. In the case of high enterocele, the Douglas pouch was mobilized, shortened by a purse string, and the sacrouterine ligaments, cervix and anterior rectal fasciae united to close the hernial opening.

Uterine prolapse in the majority of instances was treated by ventrofixation, using either the intraperitoneal or extraperitoneal technic.

For incontinence, the Kelly technic has usually been employed, bringing together in the midline the tissues at the base of the bladder and over these fasciae the pubocervical tissues.

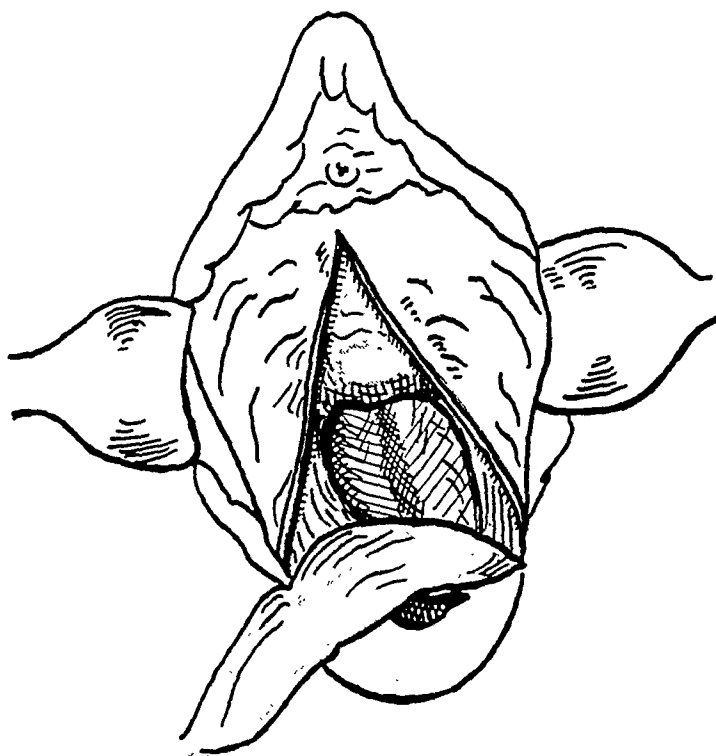


Fig. 2.—Fothergill operation. This and the following figures illustrate the anterior denudation, vesicocervical band cut across, bladder pushed back showing pubocervical tissues laterally.

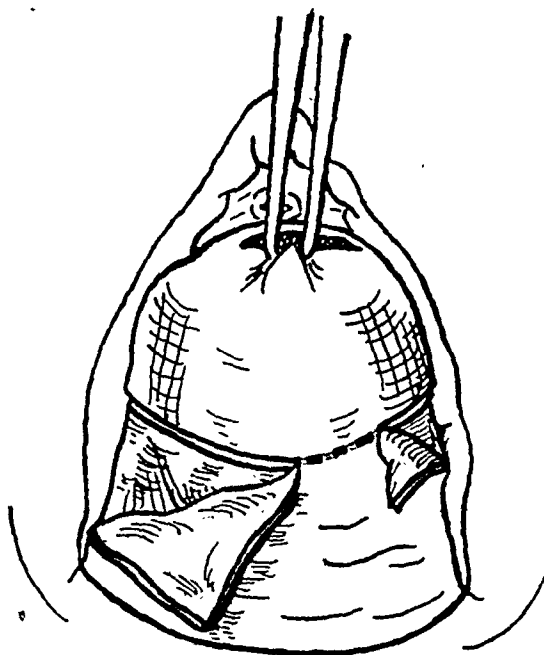


Fig. 3.—Posterior line of incision to expose pouch of Douglas and sacrouterine ligaments.



For special indications, various other operations have been employed. For large isolated billiard ball cystocele, an occasional interposition operation was used. In women of advanced age, with complete prolapse, the Le Fort operation has proved very satisfactory. In 1929 I reported on a modification of Polk's intraabdominal cystocele operation.<sup>3</sup> This operation is of value where hysterectomy must be performed, usually for fibroids of the uterus, and in which to overcome an apparent or potential prolapse, the cervical stump requires ventrofixation in the abdominal wall. Before performing the fixation, the cystocele

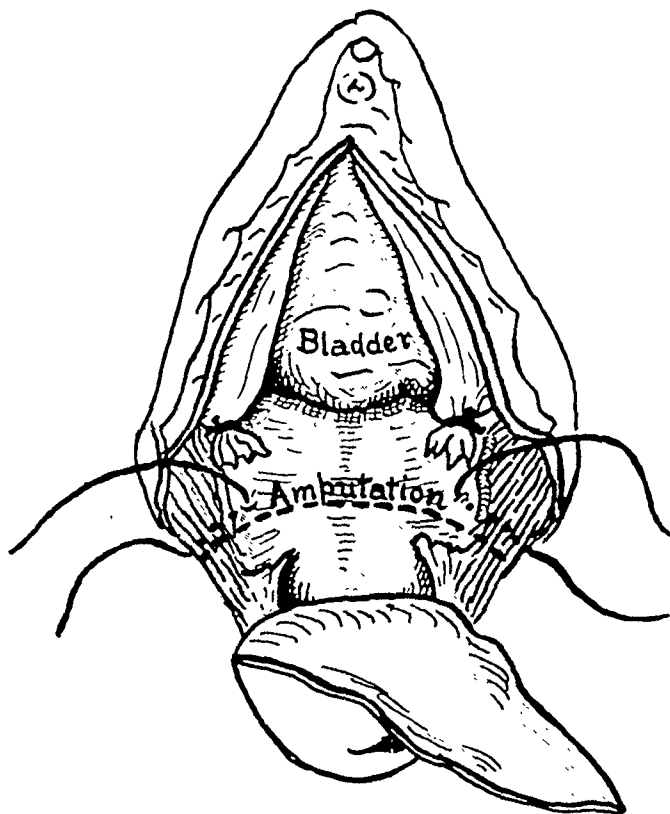


Fig. 4.—Pubocervical tissues ligated and cut away from cervix. Lateral hemostatic sutures (not tied) traverse cardinal ligaments and include uterine arteries. Line of amputation indicated.

can be cured by the Polk technic. The operation, however, does not lend itself to general use in the treatment of prolapse.

Realizing that better results should be obtained, in the last two years I have occasionally resorted to vaginal hysterectomy as advised years ago by Fritsch,<sup>4</sup> and more recently advocated by Mayo,<sup>5</sup> Ward,<sup>6</sup> and others.

The history of vaginal hysterectomy for prolapse is an interesting one. The first reference to the operation appears to be Choppin\* of New Orleans, who in 1860, after repeated unsuccessful resection and

\*Choppin: New Orleans Med. News & Hosp. Gaz. 7: 939, 1860, and South J. M. Sc. 1: 622, 1866.

plastic repair, performed vaginal hysterectomy with removal of part of the vaginal mucosa by means of the ecraseur. The vault was closed with silver wire and lead clamps without drainage. Cure was affected, the patient dying four years later from dysentery.

In Germany Freund, Fritsch, Asch, et al., reported results during 1889.

In this country the operation was practiced sparingly until the last decades when it has again gained in popularity.

At the outset, I followed the directions given by Mayo and Ward,

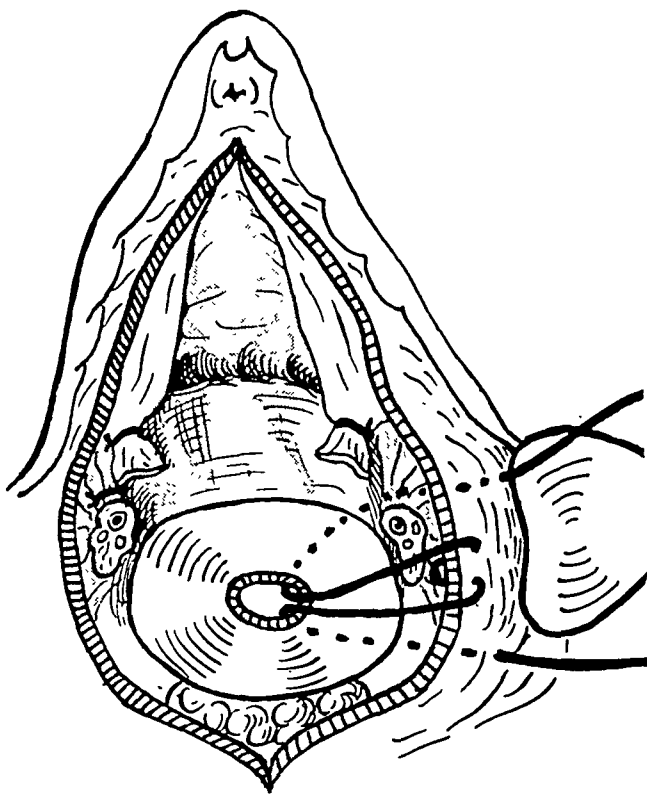


Fig. 5.—Cervix amputated. One lateral cervical suture passed including cardinal ligaments, cervix and mucosa of left fornix.

including the union in the midline of the stumps and their suture to the pubis. After becoming more familiar, not only with the operation but also with its results, I have found it unnecessary to resort to this more or less complicated technic and find that a rapid vaginal hysterectomy, with appropriate resection of the entire thickness of the anterior vaginal wall, suffices. The two upper stumps are released but extraperitonealized, all attention being focused upon the lower stumps containing the base of the broad ligaments (cardinal ligaments) to which the vault of the vagina, including not only the mucosa but also the fascial structure (pubocervical tissues, sacrouterine ligaments, and posterior vaginal fornix) are approximated in the midline. This gives not only a firm vault but because of the shortening and union of the tissues, with-

out the interposition of the cervix which has been removed, raises the vault high into the middle of the pelvis and affords efficient support to the fornix as well as to the bladder. The posterior repair which concludes the operation, overcomes rectocele and descensus of the posterior vaginal wall.

As a sequel to the satisfactory result obtained in the majority of cases by vaginal hysterectomy, it followed naturally that my attention should be attracted to the technics so widely practiced in Great Britain, the "Fothergill" operation<sup>7</sup> which came into question in younger women in

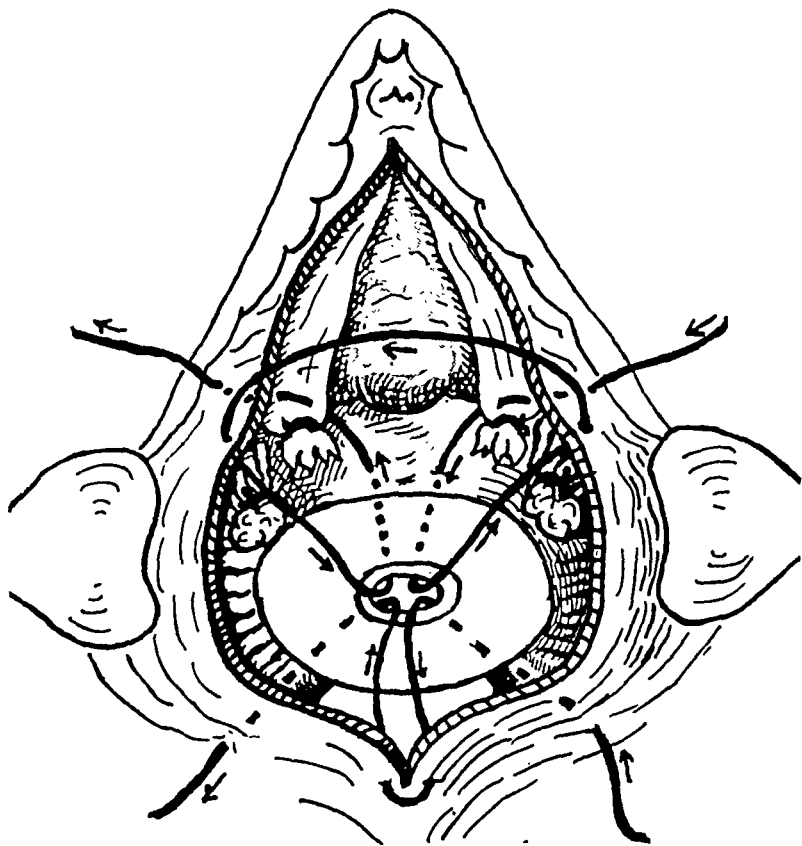


Fig. 6.—Anterior and posterior sutures passed. Anterior suture includes vaginal wall, pubocervical structures and cervix. Posterior suture includes posterior vaginal fornix, sacrouterine ligaments and cervix.

whom removal of the uterus was not indicated and was to be avoided if possible. My experience with the Fothergill operation, which dates only from the beginning of this year, has been interesting and promises to prove satisfactory because it fulfills the anatomical essentials, namely the bringing together of the bases of the broad ligaments as well as shortening of the pubocervical structures. During the writing of this paper an article from Halban's clinic by Mestitz<sup>8</sup> elaborately describes an identical procedure which Halban has practiced since 1919. This

encourages me greatly as, with the exception of Tandler and Martin, no one else has studied the anatomy of this region to the same extent as Halban.

These operations, whether we call them the Donald-Shaw-Fothergill, which were initiated in England by 1888, or Halban's, first practiced in 1919, may solve our difficulties although in special cases, as before, other technics such as those of Watkins, Wertheim, Schauta, Kielland, Le Fort, Polk, Fritsch, Mayo, Ward, will doubtless find their special application.

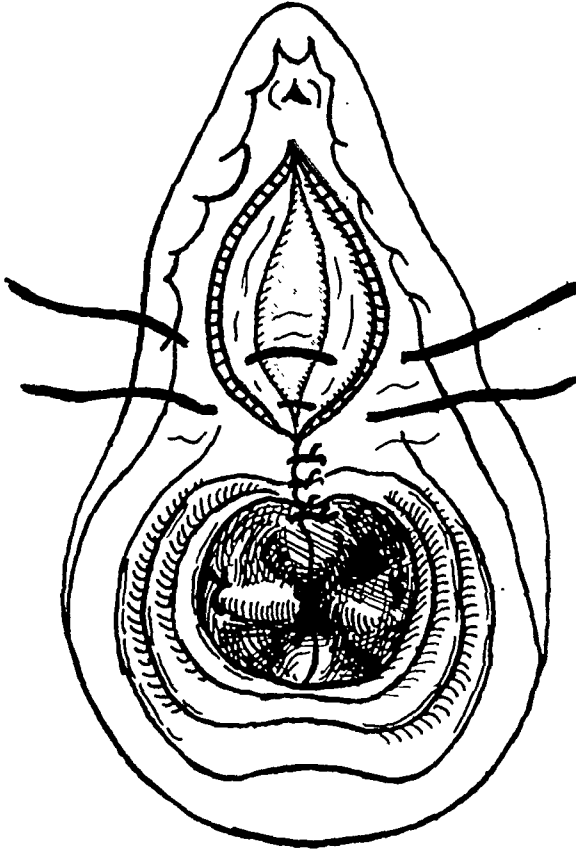


Fig. 7.—Suture of cervical stump and fornices completed. Cervix released and retracted. Two sutures have been passed through mucosa and pubocervical structures to hold back bladder.

In conclusion I would say that in my hands and those of my group, the results obtained for the cure of prolapse, are not as satisfactory, when critically examined, as those of other gynecologic operations.

This applies particularly to the cure of incontinence, the frequency of ventral hernia when laparotomy is performed, a perfect anatomical restoration in vaginal repair.

The best results were obtained in cases of rectocele and cystocele, unaccompanied by descensus.

Based upon this careful taking of stock in a considerable series, in

future I plan to continue the use of our technic for anterior and posterior colporrhaphy in cystocele and rectocele unaccompanied by prolapse.

In the absence of cystocele and presence of incontinence, not to subject patients to operative intervention unless every psychical and neurologic cause for this condition can be excluded. If operation is to be performed, I intend to use a transverse fascial strip, either free or pedicled across the neck of the bladder. In the presence of prolapse, in young women, to employ the Fothergill operation; in old women with complete prolapse, to utilize the simplified vaginal hysterectomy.

As previously stated, in the course of abdominal hysterectomy complicated by descensus and cystocele, to employ the Polk operation with ventrofixation of the stump.

In poor operative risk in the aged, as heretofore, the Le Fort operation.

The statistics gathered by Lindeman and Mayer have convinced me that no personal follow-up, except if performed over a considerable period of time by the same, preferably overcritical individuals, is of value. Follow-up conducted by means of post card, reports of outside physicians, or based on early results, are misleading and of no value.

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10 EAST EIGHTY-FIFTH STREET.

# CONGENITAL ABSENCE OF THE VAGINA AND ITS TREATMENT\*

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**C**ONGENITAL malformations of the female genitalia extensive enough to interfere with function or with normal habits are sufficiently common to warrant the serious consideration of physicians.

The developmental defects of the vagina may be grouped as follows: aplasia, atresia, hypoplasia, duplication and various combinations of aplasia, atresia, hypoplasia and duplication.

*Aplasia.*—Entire absence of the vagina is usually associated with absence or arrested development of the uterus and sometimes also of the tubes. Frank stated that in most cases of congenitally absent or defective vagina, except when a septum is present, the uterus is functionless and there are no symptoms of retained menstrual blood at puberty. In the extreme forms, the entire vagina is represented by a fibrous or fibromuscular cord situated between the bladder and the rectum with the uterus usually maldeveloped, often solid, and divided into two parts. The hymen may be absent or well developed.

*Atresia.*—The atresia may be transverse and in this plane may be complete or incomplete. Diaphragm-like membranes result from incomplete canalization of cells in one or both segments. The favorite sites are at the juncture of the lower and upper part with the middle third of the organ. On the other hand, there may be long solid areas to either side of the median line without a lumen, due to failure of canalization of a considerable portion of one müllerian duct.

Because it is difficult to explain marked developmental inhibition of the müllerian ducts, in which the uterus or upper part of the vagina is absent, but the lower third and the vulva are normal, Wharton and Masson have stated the belief that the vagina has a dual origin, the upper two-thirds being derived from the müllerian ducts and the lower third from the external genitalia. If one accepts the view of Felix that the whole vagina develops from the müllerian ducts, there may be lateral atresia of the vagina, because one lateral half of the vagina is imperforate. Thus with uterus unicornis, a narrow, somewhat laterally situated vagina may be formed from the lower end of one müllerian duct.

*Hypoplasia.*—This condition is characterized by shortness and narrowness of the vaginal canal. The rugae and vaginal folds are flat and meager. The posterior upper vaginal pouch is shallow or absent, and the cervix points in the direction of the vaginal axis or toward the bladder. This is quantitative rather than qualitative development.

*Duplication.*—This may be considered as true duplication or pseudoduplication. Frank cited two cases of true duplication in each of which there were widely separated uteri, two vulvae, two urinary bladders and duplication of the lower part of the spinal column.

Under the group of false duplication may be considered vaginas resulting from partial or complete failure of absorption of the fused adjacent portion of the müllerian ducts, resulting in complete or partial vertical septums being left in the vagina.

\*Read at the Fifty-Seventh Annual Meeting of the American Gynecological Society, Quebec, Canada, May 30 to June, 1, 1932.

Various combinations such as atresia and duplication in the same patient are occasionally found. In the last two years I have observed six patients with complete absence of the vagina. I performed a transplantation of small bowel as described by Baldwin on five of them. As a rule the condition is not recognized until the age of puberty, as the external genitalia usually appear more or less normal. In many instances it is not recognized until marriage is contemplated. Such patients, as a rule have other anomalies of the internal genital organs, the most common of which is aplasia or rudimentary uterus with no endometrium and no

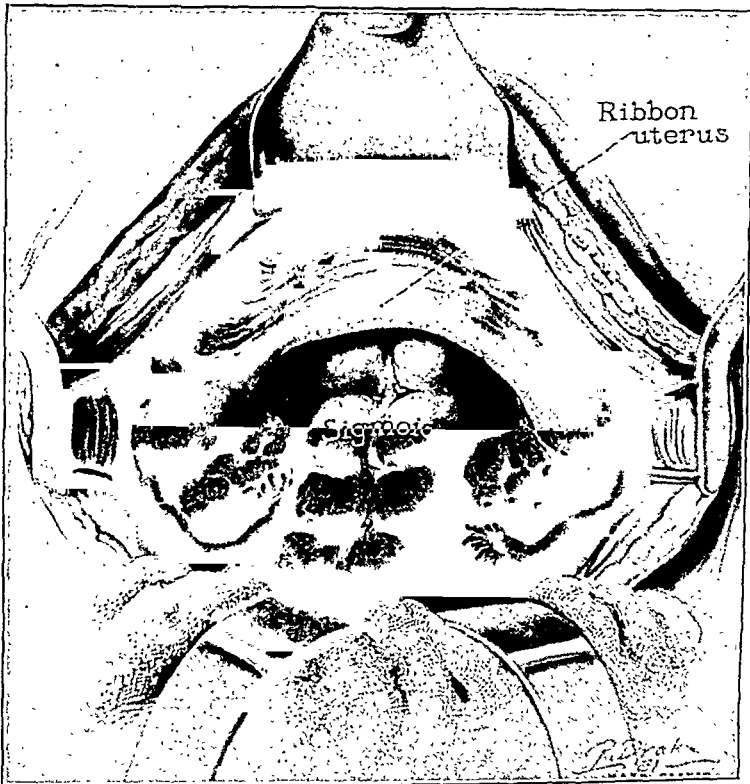


Fig. 1.—Exposure of solid rudimentary uterus. Condition usually found in complete absence of the vagina.

tendency toward the development of hematometra (Fig. 1). If the ovaries are present these patients are normal, but unless a vaginal canal can be constructed they will not be able to look forward to marriage. In many instances a marked sex complex and neurosis develop making patients very unhappy and unable to take their place in society. Several cases are on record in which the urethra has been sufficiently dilated to allow sexual intercourse. One such patient who came under my care died of infection of the urinary tract as the result of such a practice.

Of importance is the psychologic consideration of these patients. Assurance that the condition is not so very uncommon and that it, per se, will not in any way interfere with their normal health will do much to satisfy them. All operative interference should be postponed if possible

until marriage is contemplated. Many surgeons believe that surgical interference should never be advised for this condition, but when a patient with this condition makes up her mind to be married or wants the condition corrected, no amount of argument or advice will change her and suicide is often contemplated. Judin observed two such cases.

It will be possible here to give only a short description of the development of the müllerian ducts from which the entire internal genital tract of the female develops. From the fifth to the sixth week with the development of the genital glands on the mesial side of the wolffian bodies, the müllerian ducts develop on the lateral aspect of the wolffian ducts as a tubular invagination of the cells lining the coelom. The orifice of the invagination remains patent and undergoes enlargement and modification to form the abdominal ostium of the uterine tube. The müllerian ducts pass backward lateral to the wolffian ducts, but toward the posterior end of the embryo they cross to the mesial side of these ducts and end in an epithelial eminence, the müllerian eminence on the central part of the cloaca, between the orifices of the wolffian ducts; later they open into the cloaca at this situation.

From the müllerian ducts develops the entire internal female generative tract to the vaginal introitus. The müllerian ducts are at first solid and extend to the urogenital sinus as separate, unfused structures. The fusion of the lower half of the müllerian ducts is complete in the ninth week of fetal life, the vagina still being solid but the uterus composed of two hollow compartments. The septum of the fused walls forming the uterus disappears from below upward. This part of the canal is lined by a single layer of epithelium and has two hollow compartments, whereas the vagina is still solid, being composed of large cells rich in protoplasm. The uterine musculature develops about the fourth month.

In the fourth to the fifth month, the uterus and vagina acquire a single communicating lumen. The uterus and vagina are distinguished from each other by the formation of the cervix at the beginning of the fifth month. The hymen appears in the fifth month as a special differentiation of the lower vaginal segment and represents the remains of the müllerian eminence.

In the male, the müllerian ducts atrophy, but remnants of their anterior ends are represented by the appendix testis or the hydatid of Morgagni, whereas the terminal fused portions form the utriculus in the floor of the prostatic portion of the urethra.

#### OPERATIVE PROCEDURES

Two types of operation have been advised for congenital absence of the vagina: plastic flaps of skin taken from the labia or thighs as advised by Graves, Davis and Cron, Frank and Geist, Grad, and others, or resection of a portion of the intestinal tract, retaining its blood supply and implanting it in the normal situation of the vagina, as advised by Baldwin, Schubert and others. There are advantages and disadvantages in both these methods, but I believe that unless the canal is lined with mucous membrane it will not be very satisfactory. Not only is there more danger of cicatricial contraction but surfaces of skin in close apposition, unless they are kept scrupulously clean, will tend to macerate and become infected. We have all seen examples of this in a deep, funnel-shaped umbilicus, or beneath pendulous breasts or in the fold beneath a pendulous abdomen. Another disadvantage of such operations is the unnatural dry surface. Graves stated that the skin becomes soft, moist and devoid of hair in six weeks. This is probably more likely to occur



when most of the tissue is obtained from the labia than when skin from the thigh is used. On the other hand, Bumm reported a case in which hair continued to grow on the flap and it had to be removed. The chief recommendation of such operations is that they are relatively safe, but failures must be frequent. In two of the cases in which I have operated, previous plastic operations had been attempted. Furthermore plastic flaps require several surgical procedures and long hospitalization, and in case of necrosis after insertion between the bladder and rectum there is danger of a spreading infection in the retroperitoneal tissues, and any secondary surgical procedure will be more difficult.

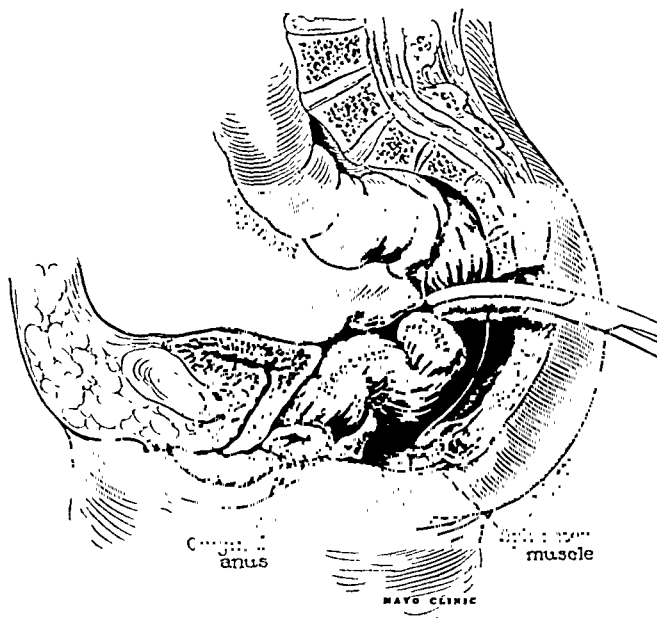


Fig. 2.—Popov-Schubert operation; utilizing rectum for vagina.

The Popov-Schubert operation consists in utilizing the lower 12 cm. of the rectum for a vagina, drawing the upper part of the rectum down through the sphincter muscles and attaching it to the skin (Fig. 2). It is a relatively safe procedure as the peritoneum is not opened, but any operation on the large bowel predisposes to local infection and sepsis, and if the newly constructed anal canal does not hold to the edges of the skin there is danger of incontinence and obstruction. However, the operation has been performed successfully by many operators in Germany. Wagner of Prague reported a case in which operation was performed at the age of thirteen years. The uterus was normal, the patient later became pregnant, and a child was delivered normally. The operation has much to recommend it, and Schubert claims a mortality rate of 3.2 per cent in 95 reported cases.

In 1904, Baldwin suggested using a segment from the sigmoid flexure to make a new vagina (Fig. 3), and in 1907 he suggested using a loop of ileum. I have operated on five patients, using the ileum, and have recently received answers to questionnaires sent to them. They are all well satisfied with the results. One of the objections to the operation is the high mortality rate, quoted by some as 17.4 per cent and by others as 6 per cent, but I feel that if proper care is taken not to make undue tension on the loop of ileum, there should be no real risk from operation, and

the mortality rate should be below 6 per cent. Another objection to this operation is the free discharge that the patients complain of, but it should be remembered that they have never been used to menstrual periods and have never had any leucorrhea; in most cases the discharge is relatively slight and never causes irritation of the skin. It can be reduced to some extent by not making the loop of ileum any longer than is necessary. In the occasional case it may not be possible to find a loop of ileum that can be brought down to the perineum, and in such event it will be advisable to use a loop of sigmoid or close the abdomen, and later to perform a Popov-Schubert operation, using the ampulla of the rectum. If the loop of sigmoid is used, the result should be satisfactory as there would be no increase in mucus secretion, but the risk of the operation would be definitely greater than if the small bowel is used.



Fig. 3.—Construction of vagina from a loop of sigmoid.

#### ABSTRACTS OF CASES

CASE 1.—A divorced woman, aged nineteen years, came to The Mayo Clinic October 21, 1929. Her chief complaint was congenital partial absence of the vagina. The patient had been married in June, 1928, at which time the congenital defect was discovered. In July, 1928, an attempt was made to dilate the vagina without much success. The patient had never menstruated.

Examination disclosed a short vagina, measuring about 5 cm. Otherwise, all characteristics were apparently normal and sexual sensations were normal. The urinalysis was essentially negative and the hemoglobin was 14.1 gm. in each 100 c.c. of blood. The Wassermann reaction of the blood was negative. Although the patient was divorced she wanted the operation as she felt that it would make a difference in her mental reaction toward life.

October 24, 1929, a Baldwin type of operation was performed. The tubes and ovaries were normal. On each side of the pelvis was a small, rudimentary uterine horn, apparently without mucous membrane as there was no tendency toward hematometra. Convalescence was uneventful and the patient was dismissed November 20, 1929. Before leaving the clinic she was instructed in the use of a

dilator; the use of this did not cause pain or discomfort. She stated in a letter dated October 28, 1931, that her health is practically on a par with what it had been before the operation. Her only complaint was of a discharge, noticeable chiefly during the process of digestion. She has not yet remarried, but she stated that she uses the dilator only at rare intervals, and with ease.

CASE 2.—A single woman, age twenty-three years, came to the clinic November 4, 1929. She complained chiefly of amenorrhea. At the age of fourteen years she began to have irregular cramps low in the abdomen, occurring at intervals of two or three months. At the age of sixteen years the cramps became regular every month. However, menstrual flow had not appeared. The cramps were likely to last from three to five days, occasionally confining the patient to bed. In 1922 appendectomy had been performed because of these pains.

Examination disclosed congenital absence of the vagina, hematometra and double uterus. The urinalysis was essentially negative and the hemoglobin was 12.5 gm. for each 100 c.c. of blood. The Wassermann reaction of the blood was negative.

November 6, 1929, exploration was carried out through a low, median line incision and a congenital anomaly was found, consisting of a double uterus widely separated on each side of the pelvis. Each side of the uterus had a normal tube. The ovary on the left side apparently was normal, but the ovary on the right contained a tarry cyst about 6 cm. in diameter. Each uterine body contained a small amount of endometrium and the cavity was dilated with retained menstrual fluid. Both parts of the uterus, both tubes and the right ovary were removed and an entero-anastomosis was made between two loops of ileum close to the ileocecal valve with the idea of using this part of the bowel to make a new vagina later.

November 20, 1929, a Baldwin type of operation was performed. After an uneventful convalescence the patient was dismissed from the clinic December 11, 1929. June 2, 1930, the patient wrote that since her return home she had married and was pleased over the result of the operation. We heard from her again about November 25, 1931, at which time she stated that the results had been very satisfactory but that there was considerable discharge.

CASE 3.—A single woman, aged twenty-eight years, came to the clinic August 6, 1930. Ten years before this a local physician had examined her because of amenorrhea, and absence of the vagina and uterus was discovered. The patient had not experienced pelvic cramping or pain, but occasionally had noticed soreness of the breasts.

Examination showed that the external genitalia were well developed. The vagina was congenitally absent, there was only a small pocket about 1.5 cm. deep. The ovaries and uterus could not be palpated. Urinalysis was negative, and the hemoglobin was 16.4 gm. for each 100 c.c. of blood. The Wassermann reaction of the blood was negative. The patient contemplated marriage and operation was advised.

August 29, 1930, a Baldwin type of operation was performed. Apparently normal tubes and ovaries and a ribbon-like uterus were found. A small amount of tissue on each side of the pelvis did not contain endometrium. Convalescence was uneventful and the patient was dismissed feeling well September 16, 1930, but the discharge of mucus through the vagina was free. In February, 1931, we received a letter from the patient in which she stated that she had married and that her married life had been extremely happy. She did not mention a discharge.

CASE 4.—A widow, aged thirty-eight years, came for consultation October 6, 1930, because of lack of a vaginal orifice. She had never menstruated and had not had sexual intercourse. Plastic operations on the vagina had been attempted twice.

Examination did not disclose abnormalities, except congenital absence of the vagina and a great deal of scarring about the vulva. Urinalysis was essentially

negative and the hemoglobin was 12.6 gm. for each 100 c.c. of blood. The Wassermann reaction of the blood was negative.

October 9, 1930, a Baldwin type of operation was performed. A vaginal canal about 2 cm. long, the result of two previous plastic operations on the vagina, was found. Tubes and ovaries apparently were normal. The two halves of the uterus were widely separated; they were lying along the pelvis and were united in the middle by a fibrous ridge and did not contain endometrium. Convalescence was uneventful except for pyelonephritis on the left side, but at the time the patient left the hospital this had cleared. She was dismissed from observation December 3, 1930, at which time the operation appeared to be successful. A letter from the patient dated October 24, 1931, stated that the operation had been successful and that the discharge is only about half as much as that which immediately followed operation. She has not remarried.

CASE 5.—A single woman, aged twenty-four years, came to the clinic June 16, 1931, because of congenital absence of the vagina. She was otherwise perfectly developed and stated that she had normal sexual sensations. She had not, however, menstruated.

Urinalysis was negative and an examination of the blood showed a hemoglobin of 12.9 gm. for each 100 c.c. The Wassermann reaction of the blood was negative.

A Baldwin type of operation was performed June 20, 1931. On rectal examination evidence of a uterus could not be found, but at the time of operation a small amount of uterine tissue was discovered on each side of the pelvis with apparently normal tube and ovary attached. An endometrial cavity in the uterine tissue could not be found. Convalescence was uneventful. The patient was dismissed from observation July 30, 1931, and given two vaginal dilators, 2.5 cm. and 3.5 cm., with instructions to insert a dilator once or twice a day and leave it in place twenty minutes or half an hour each time. She was married September 1, 1931, and in a recent letter she stated that she is pleased with the result of the operation and has had no trouble with her married life. Her only complaint is the discharge, which she thinks is definitely less than when she left the clinic.

#### COMMENT

This operation must be looked on as a major procedure, but for surgeons accustomed to operating on the gastrointestinal tract, the mortality should not be higher than for other benign conditions. The operation should be completed in from one hour to one and one-half hours, and the patient should not be in the hospital more than four weeks. The steps of the operation are as follows:

1. By blunt dissection a cavity is made in the soft tissue between the bladder and rectum up to the peritoneum and packed with gauze. In most cases the external genitalia are more or less normally developed and dimpling represents the position of the vagina.

2. The abdomen is opened and a section of small bowel about 20 to 25 cm. long with mesentery sufficient to allow it to reach to the perineum is resected. As a rule, this loop will be found in the lower part of the ileum. The continuity of the intestine is reestablished preferably by suture; side-to-side or end-to-side anastomosis is just as satisfactory and a little safer than end-to-end anastomosis on account of some interference to the blood supply as the result of freeing the mesentery of the detached section or as result of traction. The ends of the detached section are securely closed by purse-string sutures or by end-to-end union, and the low point of the loop is then drawn down into the excavation made between the bladder and

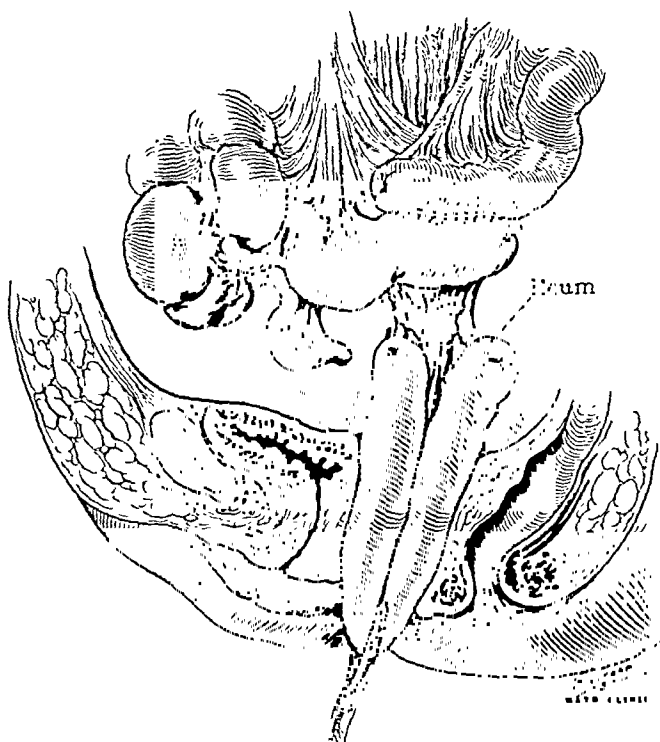


Fig. 4.—Loop of bowel drawn down in the space made for vagina (Baldwin). Blood vessels may be noted in the edge of the mobilized mesentery.

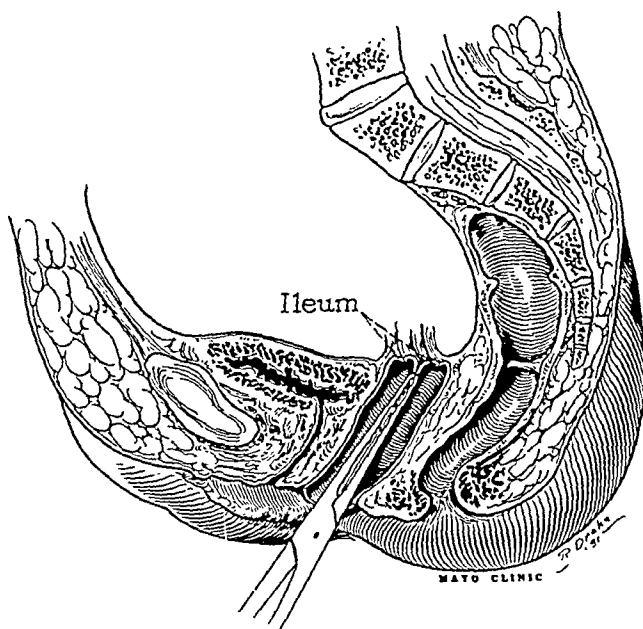


Fig. 5.—Clamps applied to destroy the septum in the newly constructed vagina (Baldwin).

rectum and the mobilized loop of ilium covered by peritoneum as thoroughly as possible (Fig. 4). To avoid interference to the blood supply it is advisable to leave large vessels at each end of the resected loop rather than one in the middle where the tension is greatest.

3. The abdominal wound is closed.

4. The presenting loop of bowel in the perineal wound is opened and securely stitched to the skin of the vulva by interrupted silk sutures.

5. The two sections of the bowel are lightly packed with sterile gauze.

6. In ten days or two weeks the septum between the two sections is destroyed by applying two forceps to it and allowing them to remain in place until they cut through (Fig. 5).

7. After twenty-one days a dilator about 3.5 cm. in diameter should be inserted for two hours each day for several weeks, or until marital relations are satisfactory.

### SUMMARY

Congenital absence of the vagina is a rare condition, but is common enough to warrant serious consideration.

Handling of cases from the psychologic standpoint is important, and operation should never be urged.

Operation should not be advised until marriage is contemplated unless hematometra develops as the result of retained menses in a more or less normal uterus. If patients insist, operative correction is justifiable at any time.

Two types of operation, the use of skin flaps or sections of the bowel may be employed. I believe that a section of small bowel used as advised by Baldwin gives the best functional results, and although a more dangerous operation, it is relatively safe when properly done. It is, moreover, justifiable.

A dilator should be used until healing is satisfactory.

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# THE TREATMENT OF GONOCOCCAL INFECTIONS BY ARTIFICIAL (GENERAL) HYPERTHERMIA\*

## A PRELIMINARY REPORT

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FOLLOWING the results obtained in the treatment of general paresis by infection with malaria, the treatment of this disease has been undertaken by raising the body temperature by artificial means and maintaining this for a period of some hours—artificial, generalized hyperthermia. Other types of disease have also recently been subjected to this principle of therapy with some degree of success.

It was found in our laboratory (Carpenter et al.) that of fifteen strains of gonococci studied, many of these could be killed by subjecting them to a temperature of  $41.5^{\circ}$  C. for a period of from five to eight hours in a water-bath, though a few strains required an even longer period of time than this, occasionally as long as twelve hours being necessary. From previous observations, as yet unpublished (Warren et al.), on the treatment of general paresis and other conditions, it was found that when certain precautions were observed, the human body tolerated very well a temperature artificially elevated to  $41.5^{\circ}$  C. and maintained at that level for from five to seven hours. The shorter period of five hours was, however, the one most frequently employed and was better tolerated than the longer period.

With these facts demonstrated, it seemed logical to expect that the usual strains of gonococci could be destroyed in the body by making use of this principle, subjecting the infected woman to an artificial general hyperthermia of  $41.5^{\circ}$  C. ( $106.7^{\circ}$  F.) and maintaining this for several hours.

We present herewith a preliminary report on the observations made and the results obtained following this line of therapy in a small group of patients.

### TECHNIC OF THE PROCEDURE

As at present carried out, preliminary sedatives are given, and these must be carefully chosen. We have found it most satisfactory to administer sodium bromide 2 gm. and barbital 0.650 gm. two hours before the treatment is begun. Chloral hydrate 0.486 gm. is given by mouth at the beginning of the treatment and this latter may be repeated three hours later. Following this medication the patients usually rest or sleep quietly during the period of hyperthermia. During treatment the patient is encouraged to drink water freely while awake. The patient is placed lying on a cot in a well insulated cabinet, the head being allowed to remain outside.

\*Read at the Fifty-Seventh Annual Meeting of the American Gynecological Society, May 30 to June 1, 1932, at Quebec, Canada.

The temperature of the air in the cabinet surrounding the patient's body is heated by means of several carbon filament lamps totalling about 650 watts. The body temperature is raised by passing diathermy current through the thorax between block tin electrodes held in place by a many-tailed binder. The elevation of the body temperature by the short-wave (30 meters) radiotherm apparatus is equally efficient. After the desired temperature level has been attained ( $41.5^{\circ}\text{C.}$ ) as indicated by a rectal thermometer, and which will require an hour and three quarters, the current is shut off and the electrodes removed. The body temperature can then be easily and accurately maintained by means of the light bulbs in the cabinet, turning them on or off as indicated. With a well insulated cabinet, heat loss from evaporation of sweat is minimal, and may be further reduced by increasing the humidity of the air in the cabinet by placing an open vessel of water in it. After the patient has been subjected to high temperature for the desired length of time, usually five hours, the lights are shut off, the cabinet opened, and the patient's

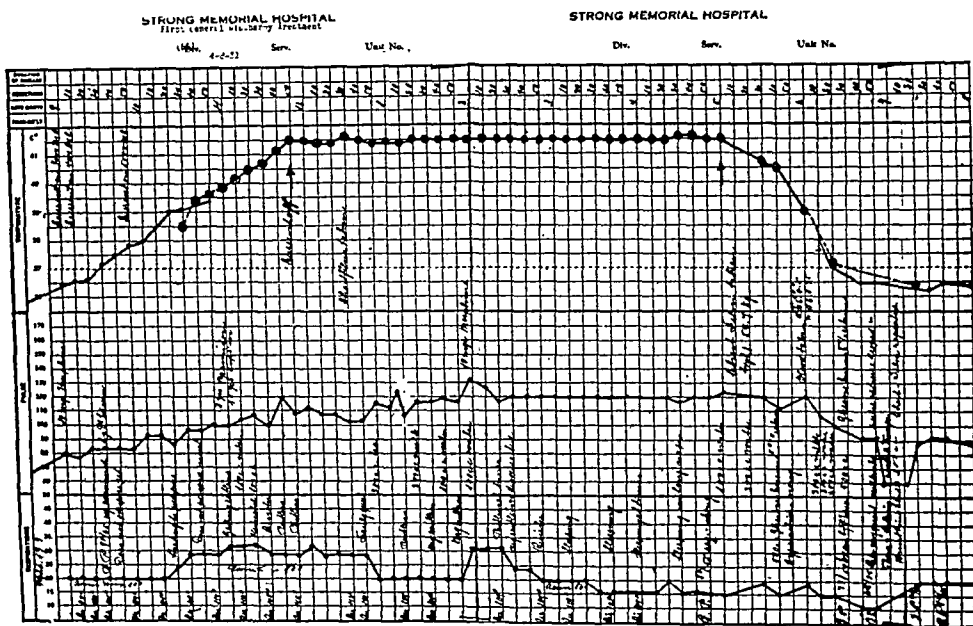


Chart 1.

body exposed to the room air. The resulting fall in temperature may be expedited by exposing the patient's body to a stream of air from an electric fan. So long as the skin temperature does not fall  $3^{\circ}\text{C.}$  below the general body temperature, no discomfort is experienced. One to one and a half hours will be required for restoration of normal temperature depending on the obesity of the patient.

The general reaction of a patient during this form of therapy is comparable to that observed in any patient with a high fever. Chart 1 presents typical temperature, pulse, and respiration curves. (The vaginal temperature, as measured by a mercury thermometer is consistently  $0.1^{\circ}\text{C.}$  or  $0.2^{\circ}\text{C.}$  below the rectal temperature.) The blood pressure at first shows a slight rise from 10 to 20 mm. Hg, but after the temperature has reached its maximum, a steady gradual drop occurs to 80/40 or 70/40. Should the systolic pressure fall to a lower level for more than a few minutes and not respond to the administration of caffeine, the treatment should be terminated. Occasionally, the ex-



citable patient may show some degree of delirium. An occasional patient may also develop herpes about the lips. There is a marked loss of weight during the treatment at times amounting to as much as four or five kilos, which is usually regained in from seven to ten days. The vaginal discharge is increased to a marked degree, as much as 200 c.c. resulting during the course of treatment. In three of our patients slight superficial burns occurred from contact with the electrodes.

An important effect of the treatment is a marked leucocytosis, the leucocyte count averaging 15,000. Associated with this is a very active phagocytosis which can be demonstrated by vaginal smears taken from time to time during the treatment. This stimulation of the normal defense mechanism is undoubtedly an important factor in the results obtained.

On account of the general effect on the patient, this line of therapy is distinctly contraindicated in the presence of vascular or respiratory disease and also in alcoholics.

#### PRESENTATION OF RESULTS

The first patients to be subjected to this line of therapy were a small number of young women who presented evidence of a gonorrheal infection of the lower birth canal only, and in whom as far as could be ascertained there was no extension of the infection beyond the cervix. None of these patients were acutely ill, but they all presented local evidence of infection, and repeated bacteriologic examinations revealed the presence of gonococci in material obtained from the cervix or urethra. These patients had been hospitalized on account of the fact that they were inmates of a shelter for delinquent girls and were considered a menace to the other inmates.

There were six patients in this group. Five had received local treatments consisting of the application of strong (20 per cent) mercurochrome or tincture of metaphen or both to cervix, urethra, and vagina for a length of time varying from eighteen days to several weeks. In spite of these prolonged treatments, repeated bacteriologic examinations revealed gonococci to be present. They were then subjected to general hyperthermia. One of this group was so treated without having had any local treatment previously.

Following treatment by general hyperthermia, daily smears were taken from the cervix and urethra, also occasional cultures during the patients' stay in the hospital. After leaving the hospital, they were followed for varying lengths of time, repeated bacteriologic examinations being made particularly postmenstrual when possible.

In two of these patients the follow-up is admittedly of too short a duration, but this was unfortunately unavoidable. In three of the six patients treatment by general hyperthermia for five hours at 41.5° C. resulted in immediate and complete disappearance of gonococci from the cervix and urethra. In three others gonococci could still be found,

so the treatment was repeated several days later. In two instances, the second treatment resulted in complete disappearance of the organisms, but in the third, organisms could still be found after the second treatment. This one must therefore be regarded as a failure. In trying to ascertain the reason for this failure, it was found that a culture of the organisms obtained from this patient when placed in the water-bath required seven hours at  $41.5^{\circ}$  C. before it was killed, the failure obviously being due to the fact that she was infected with a strain of organisms presenting greater heat resistance.

However, following the general hyperthermia, a short period of local treatment with tincture of metaphen resulted in negative smears. This fact suggests that the organisms may at least have been considerably attenuated by the treatment.

A brief outline of the patients in this group may be presented as follows:

CASE 1.—(Unit No. 44217) Local treatments for eight weeks with no result. General hyperthermia for five hours at  $41.5^{\circ}$  C., gonococci still present. General hyperthermia repeated ten days later for five hours at  $41.5^{\circ}$  C. Repeated examinations during next eight weeks revealed no gonococci.

CASE 2.—(Unit No. 55373) Excision of Bartholin's gland and local treatments for eighteen days, smear still +. General hyperthermia for five hours at  $41.5^{\circ}$  C. Repeated examination in the next four weeks failed to show gonococci. The menstrual period which was due to occur during this patient's stay in the hospital failed to appear and at present she is approximately four months' pregnant. Therapy was apparently carried out on her during the very early stages of her pregnancy without harmful results. Subsequent examinations during four months after treatment failed to show gonococci.

CASE 3.—(Unit No. 44540) Local treatments for twenty-six days without effect. General hyperthermia for five hours at  $41.5^{\circ}$  C. Smear next day +; succeeding ones negative. General hyperthermia for five hours at  $41.5^{\circ}$  C. repeated twelve days later. No gonococci demonstrated during the next eight weeks.

CASE 4.—(Unit No. 55066) Local treatments for eighteen days without effect. General hyperthermia for five hours at  $41.5^{\circ}$  C. No gonococci found during the next week. Result apparently good, but the follow-up is defective.

CASE 5.—(Unit No. 16972) No local treatments, gonococci present. General hyperthermia for five hours at  $41.5^{\circ}$  C. No gonococci found during the next five days. Result apparently good but the follow-up is too short.

CASE 6.—(Unit No. 23475) Local treatments for twenty-six days with no effect. General hyperthermia for five hours at  $41.5^{\circ}$  C. Smears still +. General hyperthermia for five hours at  $41.5^{\circ}$  C. repeated fifteen days later (postmenstrual). Smears still +. Failure due to the fact that this was a more resistant strain, requiring seven hours at this temperature to cause its death. Smears, however, became negative after four local treatments with tincture of metaphen—apparently the organisms were at least attenuated.

Encouraged by the results obtained in this group of patients, a small number of women who showed definite evidence of tubal involvement of an acute or subacute type in addition to signs of infection in the lower birth canal were subjected to this type of therapy.

All of these had had local and palliative treatment prior to being subjected to general hyperthermia for a varying length of time. Following this each was subjected to a single general hyperthermia treatment at 41.5° C. for five hours except in two instances when it was reduced to three hours, once on account of the violence of the patient and once on account of the poor reaction of the patient. There were 9 patients in this group, all being hospital cases. In 6 of them the results obtained left little to be desired, in 2 the result can only be regarded as partially successful, while in another it resulted in failure. The failure may be fairly attributed to a too short duration of treatment. The important features in this group of patients may be briefly outlined as follows:

CASE 7.—(Unit No. 13766) Puerperal exacerbation of gonorrheal infection with tubal involvement. Local and palliative treatment for twenty days, symptomatically improved but gonococci still present. General hyperthermia resorted to. Followed at intervals for four months. No gonococci found and no gross evidence of pelvic disease.

CASE 8.—(Unit No. 52099) Evident tubal involvement but no grossly palpable masses. Local and palliative treatment for two weeks with some improvement but gonococci still present. General hyperthermia. Followed for four months. No gonococci found, slight residual thickness of one tube.

CASE 9.—(Unit No. 54995) Bilaterally palpable tubes and mass on one side 5 by 6 cm. Local and palliative treatments for six weeks. Gonococci still present, and little if any change in the pelvic findings. General hyperthermia. Followed for six weeks. No symptoms. No gonococci found, and no palpable masses at the end of that time.

CASE 10.—(Unit No. 55196) Evidence of tubal involvement but no grossly palpable masses. Local and palliative treatment for eighteen days. Improved but gonococci still present. General hyperthermia. Followed for one month. No gonococci found, no palpable abnormalities of tubes.

CASE 11.—(Unit No. 57871) Bilateral tuboovarian masses. Local and palliative treatments for five weeks. Improved but gonococci still present and little change in the size of the masses. General hyperthermia. One week later no symptoms and masses barely palpable, no gonococci found. Followed for a month. No gonococci found. Pelvic findings negative at the end of that time.

CASE 12.—(Unit No. 26290) Puerperal exacerbation of gonorrheal infection with acute tubal involvement. Local and palliative treatment for five weeks. Improved but gonococci still present. General hyperthermia. Followed for ten days. No gonococci found. Pelvic findings negative. Result apparently good but the follow-up is too short.

CASE 13.—(Unit No. 49940) Bilateral tuboovarian masses. Febrile for twenty-four days. Local and palliative treatment for seven weeks. General hyperthermia. Followed for one month. No gonococci found. Symptoms relieved but masses still present. This is only considered a partial success. Seen later gonococci found. Evidence obtainable points to a reinfection by exposure.

CASE 14.—(Unit No. 48415) Tubal involvement but no grossly palpable masses. Local and palliative treatment for six weeks. General hyperthermia for three hours only. Patient quite violent. Followed for four weeks. No gonococci found

in spite of incomplete treatment. Three months later gonococci present. Pelvic abscess drained. Definite evidence of reinfection obtained.

CASE 15.—(Unit No. 40872) First had a puerperal flare-up of a gonorrheal infection. Palliative treatment, improved. Several readmissions on account of reinfection during the next fifteen months. At present large bilateral tuboovarian masses and gonococci present. General hyperthermia for three hours only on account of poor reaction of patient with marked drop in blood pressure and unusual acceleration of pulse rate. Masses unchanged, gonococci still found. Failure on account of too short a period of treatment. This patient will require surgical treatment.

In two patients in our series the pelvic infection was complicated by the presence of a gonorrheal arthritis. In each instance the symptoms subsided entirely after they were subjected to general hyperthermia, one patient receiving two treatments while only a single treatment was administered to the other. The salient features in these two patients may be briefly outlined as follows:

CASE 16.—(Unit No. 45292) Showed the stigmata of a gonorrheal infection on pelvic examination but no organisms were found. Gonorrheal arthritis of left ankle and right wrist present. General hyperthermia for five hours at  $41.5^{\circ}$  C. followed by improvement. Repeated eighteen days later followed by rapid disappearance of symptoms. One smear +, immediately after treatment all others negative. Became pregnant a few weeks after last treatment. Spontaneous delivery, no exacerbation in puerperium, and repeated examinations failed to show gonococci.

CASE 17.—(Unit No. 55134) Active gonorrheal infection of lower birth canal and associated gonorrheal arthritis of right wrist. Excision of Bartholin's gland. Local and palliative treatment for twenty-six days. Gonococci still present. General hyperthermia. Followed for one week. Rapid improvement of arthritis. No gonococci present. Gonococci subsequently found. Reinfection admitted.

In only three cases presenting chronic salpingitis or showing the residual effects of an old acute process was this type of therapy employed. Two were quite evidently benefited by it, while the third showed no improvement in symptoms whatsoever. The results obtained in these patients may be briefly outlined as follows:

CASE 18.—(Unit No. 58973) Presented the stigmata of gonorrheal infection but no organisms found. Small bilateral tuboovarian masses present, considerable lower abdominal pain. Palliative treatment for sixteen days, not improved. General hyperthermia for five hours at  $41.5^{\circ}$  C. Five days later no pain, some decrease in size of masses. Two weeks later lateral masses almost entirely gone, no symptoms, evidence of adherent appendages.

CASE 19.—(Unit No. 59699) Stigmata of gonorrheal infection but no organisms found. Pelvic pain. Uterus retroverted and adherent, small unilateral mass. No palliative treatment. General hyperthermia for five hours at  $41.5^{\circ}$  C. Five days later pain relieved. Week later, greater motility of pelvic organs on examination.

CASE 20.—(Unit No. 48610) Stigmata of gonorrheal infection but no organisms found. Persistent right-sided pain. Thickening found in both tubes and a small right-sided mass. Long course of palliative treatment in out-patient department. General hyperthermia for five hours at  $41.5^{\circ}$  C. Symptoms not relieved. Operation six weeks later. Cystic right ovary enmeshed in the most filmy of adhesions about

right tube. Left appendages normal. Right salpingo-oophorectomy and removal of normal appendix, followed by smooth convalescence and relief of symptoms.

This case is of particular interest on account of the opportunity permitted to examine the pelvic structures some time after treatment. The adhesions, though fairly numerous, were of the most filmy type. Microscopically the tubal mucosa appeared normal. Whether the adhesions were more dense before treatment or not, it is impossible to say.

#### SUMMARY AND CONCLUSIONS

The results obtained in twenty women who presented various forms of gonorrheal infection and who were treated by general hyperthermia are herewith presented. The results on the whole have been satisfactory and generally resulted in a rapid disappearance of symptoms as well as a disappearance of the organisms. The failures in this series have been due to either deficient treatment, or to the fact that the particular strain of gonococcus encountered was more resistant to heat than the average strain of organisms is. A point we would emphasize is that even in the failures we have at no time observed any evidence which would point to an exacerbation of the condition present, but rather the reverse held true.

This series is much too small to permit of any far reaching conclusions being drawn, and we do not recommend this procedure at present as a routine procedure in the treatment of gonorrheal infections. Rather, we present this preliminary report as a clinical demonstration of the fact, established in the laboratory, that the usual strains of gonococci can apparently be destroyed in the body after exposure to high temperature for definite lengths of time. For clinical application the temperature and duration of therapy must be such as to be safely tolerated by the patient.

Encouraged by the results obtained in this small series, we propose to continue this work and hope to develop a technic which will be simpler and more easily tolerated by the patient. Further observations should also permit us to decide more accurately the type of pelvic lesion and the stage of the disease which will be most amenable to this form of therapy. No doubt some women will be found to be infected with strains of organisms which are unusually resistant to heat, and in whom therefore this line of therapy will prove to be impracticable.

THE PRESENT POSITION OF VERSION AND EXTRACTION\*  
AN ANALYSIS OF THE SHIFTING INCIDENCE OF VERSION AND EXTRACTION, HIGH FORCEPS, AND CESAREAN SECTION AT THE  
MICHAEL REESE HOSPITAL

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OPERATIVE obstetrics is steadily gaining recognition as a form of specialization essential to the practice of sound obstetrics. The successful termination of a delivery with due consideration for the maximum safety of mother and fetus depends upon a variety of factors, an intimate knowledge of the anatomic and clinical background of the patient by prenatal survey, a true evaluation of the problems which may arise in the course of labor, and the intelligent application under proper aseptic conditions of such operative procedures as may be indicated.

In recent years there has been a noticeable increase in the incidence of cesarean section in the majority of the obstetric clinics of this country. During the same period, version and extraction has, in the main, shown a definite decrease, although in some few clinics the operation has increased in popularity and frequency. Delivery by high forceps has everywhere shown a decrease.

A cursory survey of the incidence of these three operations in the Michael Reese Hospital during the past ten years revealed a decided increase in the number of cesarean sections and a 50 per cent reduction in the incidence of both version and extraction and high forceps. Convinced of the value of version and extraction and its extreme suitability under appropriate conditions, a critical analysis of the results obtained by this operation was undertaken and compared with the results obtained by high forceps and by cesarean section.

The period studied was the ten years from 1922 to 1931 inclusive, during which time, 15,136 women were confined at the Michael Reese Hospital. This included all service patients and all private patients of staff men. Of these, 156 or 1.03 per cent were delivered by version and extraction. From the New York Lying-In, Markoe reports an incidence of 2.23 per cent in 60,000 consecutive deliveries. Krukenberg reports 1.6 per cent from the Bonn clinic for the period 1912 to 1929. Good from the Boston City Lying-In Hospital reports 3.24 per cent over a ten-year period ending with 1929. Greer gives 3 per cent for a six-year period with 4668 deliveries at the Evanston Hospital. Stander reports 2 per cent incidence of version and extraction at the Johns Hopkins Hospital, and Polak reports 5 per cent incidence of version and extraction at the Long Island Hospital during 1920-30. Willets gives the incidence as 3.36 per cent in Grand Rapids.

\*Read at the Fifty-Seventh Annual Meeting of the American Gynecological Society, May 30 to June 1, 1932, at Quebec, Canada.

TABLE I. MICHAEL REESE HOSPITAL, 1922-1931

	VERSION AND EXTRACTION	HIGH FORCEPS	CESAREAN SECTION
1922	1.17 per cent	1.17 per cent	0.85 per cent
1923	1.52	1.66	0.58
1924	1.56	1.40	0.85
1925	1.70	1.86	1.24
1926	1.09	0.75	1.03
1927	0.55	0.85	3.40
1928	0.49	0.62	3.08
1929	0.77	0.33	3.85
1930	1.00	0.21	4.23
1931	0.82	0.27	4.36
Total	156—1.03 per cent	148—0.97 per cent	381—2.52 per cent

During this same period 148 or 0.97 per cent were delivered by high forceps and 381 or 2.52 per cent by cesarean section.

The trend in the selection of these operations is well shown by a comparison of the first and second five-year periods. It will be observed that the incidence of version and extraction dropped 50 per cent, from

	VERSION AND EXTRACTION	HIGH FORCEPS	CESAREAN SECTION
1922-26	94—1.40 per cent	91—1.36 per cent	61—0.91 per cent
1927-31	62—0.73 per cent	57—0.68 per cent	320—3.78 per cent

1.40 per cent to 0.73 per cent. The same is true of delivery by high forceps, the incidence dropping from 1.36 per cent to 0.68 per cent. Cesarean section on the other hand increased 420 per cent from 0.91 per cent to 3.78 per cent. The total number of versions and extractions for the ten-year period was 156 and the total number of high forceps was 148. The total number of cesarean sections was 381. The 50 per cent drop in version and extraction and in high forceps and the fourfold increase in cesarean section represents not merely a shift in indications and in the replacement of version and extraction and high forceps by cesarean section but also an actual increase in the number of cesarean sections based on a widening of the indications for this latter operation.

*Parity.*—The parity of the patients delivered by version and extraction ranged from *pari i* to *para xii*. Of these 42 were *primipara*, 38 were *para ii*, 24 were *para iii*, 17 were *para iv*, 5 were *para v*, and 21 were *para vi* to *xi*.

There is a widespread feeling that the *primipara* is poorly adapted for the successful performance of this operation because of the nulliparous integrity and resistance of the lower birth canal. Potter has shown conclusively that the pelvic floor can, under surgical anesthesia, be so completely ironed out in most instances as to offer no greater resistance to the advance of the fetus than does the birth canal of the *multipara*. This preparatory overstretching of the pelvic musculature and fascia must be carried out gently but over a sufficiently long period of time to obtain the desired result. *Episiotomy* is no substitute while

perineotomy sufficiently deep to lay open the birth canal involves an extensive and unnecessary trauma to the patient.

*Duration of Pregnancy.*—The duration of pregnancy varied from twenty-eight to forty-four weeks among the 156 patients under consideration. Of these 109 were at term, 14 were postmature and the remainder were premature.

28 weeks	1	38 weeks	10
30 weeks	2	Term	109
32 weeks	5	42 weeks	4
34 weeks	6	44 weeks	10
36 weeks	9		

Postmaturity is not in itself a contraindication for version and extraction. The feasibility of the procedure depends upon the existence or degree of disproportion and can be determined by the Mueller or the Hillis maneuver.

*State of the Membranes.*—Analysis of the state of the membranes revealed that they were intact in 75 patients, recently ruptured in 51 patients, ruptured one to four hours in 11 patients, five to twelve hours in 8 patients, and over twelve hours in 11 patients.

The facility with which the fetus can be manipulated within the uterine cavity during labor depends upon the degree of anesthesia and upon the amount of liquor amnii present at the time of version. Version is among the easiest of the intrauterine operations when these conditions are satisfactorily fulfilled. It can still be carried out under deep surgical anesthesia after considerable liquor amnii has been lost. Version should not be undertaken if overstretching of the lower uterine segment and moulding of the uterus around the fetus indicate a complete loss of liquor amnii with the consequent increased risk of rupture of the uterus. This explains the apparent anomaly that version sometimes fails when undertaken only one or two hours after rupture of the membranes and may succeed twenty-four or more hours following rupture in other patients.

*Cervix.*—The cervix was completely effaced in 142 patients and incompletely effaced in 14. Dilatation of the cervix had reached 10 cm. in 94 patients and was incomplete in 62 patients. The treatment instituted consisted in manual dilatation of the cervix in 24, dilatation by bag insertion in 25 and Duehrssen's incisions in 8 patients. Fourteen women sustained cervical lacerations of sufficient degree to require repair.

While it might be anticipated that more injuries of the cervix would have occurred in a group in which there was so large a proportion of incomplete cervical dilatation together with 49 artificial dilatations, it must be remembered that 33 patients gave birth to premature infants.

Manual dilatation	24
Bag dilatation	25
Duehrssen's incision	8
Lacerations	14



The dictum that version and extraction may not be attempted except in the presence of a fully dilated or dilatable cervix carries with it the implication that the qualified obstetrician must be able to determine the safety and feasibility of artificially producing complete dilatation. Manual dilatation is applicable to the thin cervix, while for the thick cervix the choice must rest between the bag for slow dilatation and Duchrssen's incisions for rapid dilatation.

*Perineal Injuries.*—Twenty-one patients sustained first degree lacerations of the perineum, 29 a second degree laceration, and 6 a third degree or complete laceration. Of these latter, 4 occurred in multiparae and 2 in primiparae. All 6 were repaired at the time of injury and all 6 healed with good functional results. Episiotomy was done 21 times, 15 of these patients were primiparae, 14 being at term. There were 33 primiparae at or past term. Five were delivered without injury to the perineal body, 5 sustained a first degree laceration, 7 a second degree laceration, and 2 a third degree laceration. In the remaining 14, episiotomy was done.

It is an open question whether these patients would have reached a better end-result by routine episiotomy, by vaginal ironing out, or by the selective methods just described. As previously indicated, skillful ironing out of the vagina and perineum on suitably selected patients provides the best means of preserving the integrity of the vagina and of the perineal body when a version and extraction is to be performed.

*Anesthesia.*—Anesthesia was employed in every instance but one. This patient was a sixteen-year-old primipara at term who entered the hospital in convulsions and died almost immediately after admission. A version and extraction done three minutes after death had occurred, resulted in a stillbirth. Open mask ether was the anesthetic used for 98 patients. Ethylene-oxygen and ether were used 45 times, ethylene-oxygen alone twice, nitrous oxide-oxygen and ether 6 times and nitrous oxide-oxygen 4 times.

It should be noted that ether anesthesia, either alone or in combination, was used for 150 of the 156 patients in this series. Complete relaxation is the essential objective for the safe performance of version and extraction. The advantage of a combination of ethylene-oxygen with ether lies first in the ease and speed of induction of anesthesia by the ethylene-oxygen and secondly in the limitation of the use of the ether to the time of the actual performance of the operation.

*Indications.*—Version and extraction was performed 42 times for cephalic malpositions, relative disproportion and failure of engagement of the fetal head. The operation was undertaken 17 times after high forceps had failed, 16 times for failing fetal heart tones, 16 times for prolapse of the cord, 16 times for transverse presentations, and 16 times for the delivery of a second twin. Fourteen patients with placenta previa were delivered by version and extraction, 8 of these were of the marginal type, 4 of the lateral type, and 2 of the central type. Five other

patients were delivered because of premature separation of the placenta. The indications in the remaining 14 patients were face presentation 6 times, toxemia of pregnancy or eclampsia 6 times and no diagnosis in 2 instances.

Version and extraction as employed at the Michael Reese Hospital is an operative procedure based on a specific pathologic indication rather than a method of termination of labor without indication. The indications as listed above are self-explanatory in justification of the operation. One exception must be clarified. Placenta previa centralis is coming more and more to be regarded as an indication for cesarean section, but there is still room for debate as the two instances recorded above demonstrate. The one patient was a para vi in the thirty-fourth week of pregnancy and the other a para ii in the thirtieth week of her pregnancy. In each patient vaginal delivery sufficed to terminate the pregnancy and the parturient was spared the additional risk inherent in any cesarean section, especially since the degree of prematurity did not warrant this increased risk for the mother.

*Maternal Mortality.*—In this series there were 5 maternal deaths, 3.24 per cent.

1. The first death occurred in 1925. The patient was a twenty-one-year-old para iii, who had been operated upon two days before delivery at term for a right-sided acute mastoiditis following otitis media. Version and extraction was done following manual dilatation of the cervix for failing heart tones. The operation was not a difficult one and the fetus weighing 3460 gm. survived. Death occurred twenty-four hours following delivery and was apparently due to shock. Autopsy revealed a rupture of the uterus extending into the right broad ligament with severe hemorrhage. The concealed hemorrhage extended into the broad ligament and into the peritoneal cavity.

2. The second death occurred in 1926 in a twenty-six-year-old para iv who was bleeding moderately from a placenta previa lateralis. The pregnancy was at term, labor induced by rupture of the membranes and bag insertion. A version and extraction was done when cervical dilatation was complete. The fetus survived and weighed 5685 gm. The placenta was removed manually, the uterus was not packed and there was a severe and continued postpartum hemorrhage which resulted in death twenty hours following delivery.

3. The third death was that of a sixteen-year-old primipara who entered the hospital at term in 1927. She had had no prenatal care and had had several convulsions before admission. She entered the hospital in status convulsus and died ten minutes after admission. Examination showed her to have complete effacement and dilatation. A version and extraction was done three minutes after death had occurred. The fetus was stillborn.

4. The fourth death was that of a forty-two-year-old para iii who entered the hospital in her thirty-sixth week of pregnancy in a moribund state from a profuse vaginal hemorrhage. The cervix was 4 cm. dilated, completely effaced, and the membranes were intact. The cervix was dilated manually, a version and extraction done. The fetus was stillborn. The placenta was removed manually and the uterine cavity packed. Death occurred ten minutes following delivery in spite of all attempts at fluid replacement. This death occurred in 1930.

5. The fifth death occurred in a twenty-eight-year-old para i (1930) at term. There was a bilateral bronchopneumonia present for two days previous to delivery,

a caseous tuberculosis of one lung and aortic insufficiency. The cervix was completely effaced and dilated when the fetal heart tones became irregular. An immediate version and extraction was done and the fetus which weighed 3770 gm. survived. Death occurred one hour following delivery. The immediate cause of death was pulmonary edema with dilatation of the right heart superimposed on the bilateral bronchopneumonia.

Of these 5 deaths, one, that of the first patient who died following a rupture of the uterus, was directly chargeable to the operation. The second death can also be charged to the type of delivery, but in none of the others did the method of delivery play a rôle in the death of the patient. The corrected mortality for the 156 patients delivered by version and extraction is therefore 1.30 per cent.

During the same ten-year period, high forceps were used 148 times. Delivery was accomplished in 131 women and failed in 17 who were then delivered by version and extraction. This incidence of 11.5 per cent of unsuccessful attempts at delivery by high forceps suggests that the operators involved, having set the indications for high forceps delivery, were discreet enough to switch from a hopeless procedure to one that held out greater hope of survival for the fetus. Actually 16 of these 17 babies survived.

There was one maternal death in the series of high forceps deliveries, a gross mortality of 0.67 per cent. This patient succumbed to a bilateral bronchopneumonia forty-eight hours following delivery. The corrected mortality is therefore 0.0.

During this same decade there were 381 deliveries by abdominal cesarean section. There were 9 maternal deaths, a gross mortality of 2.36 per cent. One patient was operated upon while moribund from influenza pneumonia and death occurred during the operation. The fetus which was near term, survived. The corrected mortality was therefore 2.10 per cent. The remaining 8 deaths were due to postoperative infections in three instances, once to eclampsia, once to hemorrhage following premature separation of the placenta, once to myocarditis, once to uremia, and once to hemorrhage following placenta previa.

During the same decade, the gross maternal mortality among the 15,136 patients delivered at the Michael Reese Hospital was 37 deaths or 0.24 per cent.

*Maternal Morbidity.*—Table II offers a comparison of the causes of maternal morbidity in the three types of operations under consideration. Infection of various origins occurred in approximately one-third of all the patients subjected to cesarean section. This is double the frequency with which infection occurred following high forceps and two and one-half times the incidence of infection occurring after version and extraction. It should be noted further that some degree of ileus occurred in approximately 10 per cent of all cesarean section patients, while shock and postpartum hemorrhage were more prominent complications in the other types of operations. Complications, either postoperative or inci-

dental occurred in one out of every 5 patients delivered by version and extraction, in one out of every 4 delivered by high forceps, and in one out of every 2 delivered by cesarean section.

The annual average morbidity of all patients delivered at the Michael Reese Hospital is 11 per cent. The standard of febrile morbidity is the generally accepted one of temperature above 100.4° F. on two successive days or 101° F. once, excluding the first twenty-four hours post-partum. Thus far vaginal antisepsis has not been used except in a very small percentage of deliveries.

TABLE II. MATERNAL MORTALITY AND MORBIDITY

	VERSION AND EXTRACTION	HIGH FORCEPS	CESAREAN SECTION
Fever of unknown origin	5.30 per cent	9.46 per cent	7.08 per cent
Foul Lochia	3.20	2.88	13.91
Sapremia	1.28	0.67	
Wound infection with or without suppuration			8.92
Puerperal sepsis	0.64	2.01	0.78
Thrombophlebitis	2.56	1.34	1.83
<i>Total Infections</i>	12.98	16.36	32.52
Shock	1.92	2.88	
Postpartum hemorrhage	4.49	4.69	0.26
Ileus	0.64	0.00	9.76
Pyelitis	0.64	0.67	5.77
Bronchitis	0.64	0.67	0.79
Pneumonia	0.00	0.00	0.79
Acute gastric dilatation	0.00	0.00	1.05
Massive collapse lung	0.00	0.00	0.26
Evisceration	0.00	0.00	0.79
Fistula	0.00	0.00	0.26
<i>Total Complications</i>	21.23 per cent	25.27 per cent	52.75 per cent
Mortality: Gross	3.24 per cent	0.67 per cent	2.36 per cent
Corrected	1.30 per cent	0.00 per cent	2.10 per cent

Study of the sources of fever revealed a considerable group classified under the heading of "fever of unknown origin." This group represented for the most part, patients in whom enough fever occurred to require inclusion under the rigid classification of morbidity. The short duration of the fever in these instances did not permit of a source diagnosis.

The incidence of foul lochia or foul lochia with fever (sapremia) 13.91 per cent, following cesarean section seems higher than it should be. The uterus is always sutured with catgut, care being taken to place the deeper row of sutures down to but not including the uterine mucosa. The foul lochia should not therefore be charged to dissolution of the catgut but rather to mild localized infection.

*Fetal Mortality.*—As might have been anticipated, the fetal mortality following cesarean section was the lowest in the three types of operation,

3.38 per cent gross mortality and 1.04 per cent corrected mortality. The gross fetal mortality following high forceps was 8.13 per cent and the corrected fetal mortality was 7.41 per cent. Following version and extraction the gross fetal mortality was 17.28 per cent and the corrected mortality was 10.24 per cent. In connection with the high rate of fetal death after version and extraction, it must be borne in mind that this figure represents the end-results in patients with various types of pathology in whom version and extraction was frequently a desperate life-saving measure rather than an operation of choice. Moreover, 7 of these babies were definitely premature. Each of the 7 weighed less than 2200 gm.

#### SUMMARY

Version and extraction was done 156 times in 15,136 deliveries, 1.03 per cent during the decade 1922-1931. The frequency of the operation dropped 50 per cent during the second five-year period. During the same ten years, high forceps were used 148 times, 0.97 per cent, with a similar 50 per cent drop in the second five-year period. The total number of cesarean sections was 381, 2.52 per cent, with a fourfold increase in the second five-year period. These figures represent not merely a shift in indications and in the replacement of version and extraction and high forceps by cesarean section but also an actual increase in the percentage of cesarean sections based on a widening of the indications for this latter operation.

The maternal mortality following delivery by version and extraction was 1.30 per cent, by high forceps was zero and by cesarean section was 2.10 per cent. The incidence of infection following version and extraction was 12.98 per cent, following high forceps was 16.36 per cent, and following cesarean section was 32 per cent. Complications both operative and incidental occurred in 21.31 per cent following version and extraction, in 25.27 per cent following high forceps and in 52.75 per cent following cesarean section. Fetal deaths occurred in 12.82 per cent of the deliveries by version and extraction, in 7.41 per cent of those by high forceps and in 1.04 per cent of the deliveries by cesarean section.

#### CONCLUSIONS

1. The well recognized dangers inherent in delivery by high forceps, justify the 50 per cent diminution in the frequency of this type of delivery.

2. The similar decrease in the frequency of delivery by version and extraction in this series is definitely not justified.

3. The margin of safety for the parturient following version and extraction is much greater than that offered by cesarean section.

4. Cesarean section must not become a substitute for version and extraction.

# THE PROPHYLACTIC TREATMENT OF THYROID DYSFUNCTION AND THE IMPORTANCE OF BASAL METABOLISM STUDIES IN OBSTETRICS AND GYNECOLOGY\*

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THE various glands of internal secretion have been the subjects of both laboratory and clinical investigation for many years, but organotherapy when applied to patients suffering from some type of gland dysfunction continues to be more or less unsatisfactory. The outstanding exception is the group of patients with thyroid dysfunction of the deficiency type who are greatly benefited from the administration of desiccated thyroid.

Interesting experimental data are being reported from the administration of certain gland products or hormones, which indicate that progress is being made, but thus far the necessary dosage is much too expensive for the average patient since the results are of a temporary nature and the cost of the preparations too great for long continued usage. It is, therefore, fortunate that so many patients with endocrine dysfunctions are benefited from the use of desiccated thyroid which is the least expensive endocrine preparation owing to the large amount of animal material suitable for its manufacture.

The relationship of the thyroid to the sex glands as evidenced by thyroid enlargement with menstruation, puberty, pregnancy, and the menopause as well as the increased incidence of goiter in the female was recognized by the ancients. The nature of this interrelationship still remains a problem for future investigations. Both clinical and laboratory investigations suggest a close relationship between the function of the thyroid and most other glands of internal secretions. It also seems probable from a purely theoretical point of view that measures directed toward the development of a normal thyroid in the fetus may prove to be of value in securing a more normal development of other glands of internal secretion.

Fortunately, the epoch making observations and clinical experiments of David Marine have made possible an almost complete elimination of thyroid insufficiencies of the developmental type. In 1917 he reported that there is always some decrease in the iodine content of the thyroid during pregnancy and he urged the administration of iodine to prevent the hypertrophy of the thyroid which occurs so commonly among pregnant women who live in goiter areas. More recent observations of Marine and others indicate that simple goiter of the congenital type may be eliminated in a single generation, provided the mothers have proper medication during the period of pregnancy. However, it seems

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probable that it may take two or three generations of goiter prevention to eliminate the hereditary factors associated with cretinism.

Marine and Kimball after making an extensive study of the school children in Detroit and Cleveland (1924-25) started a definite program for goiter prevention in these two cities. Their studies indicated that in 1924 the children in the regular schools of Detroit showed a total goiter incidence of 36 per cent while those in Cleveland showed 34 per cent. The use of iodine as a preventive measure was begun in 1925 and has been continued although in the spring of 1926 a number of physicians opposed its use arguing that the general use of iodized salt might increase the incidence of hyperthyroidism. Detroit school physicians during the school year 1930-31 examined more than 100,000 children from the first grade through high school and reported that only 2.1 per cent showed any enlargement of the thyroid. Practically all of these enlargements were small discrete adenomas of the congenital type. Kimball and Marine examined 5,075 children in the special schools of Detroit during the same period and found a total incidence of 12 per cent with some evidence of goiter, but 97 per cent of these were only discrete adenomas or a persistent thyroglossal stalk (congenital goiter) with the remainder of the gland normal.

In Kimball's recent paper on goiter (1931) he effectively answers the arguments of those who feared that the general use of iodized salt would increase the incidence of toxic goiter by showing from the records of the Grace Hospital and the Henry Ford Hospital of Detroit that the number of goiter operations have been greatly reduced during the years since iodine in iodized salt has been used throughout Michigan.

In 1919, following the early advice of Marine, I began the administration of iodine during pregnancy to every woman who showed any evidence of thyroid hypertrophy. However, the presence of congenital goiter was observed in the newborn of some women who, not having any evidence of thyroid enlargement, did not take iodine during pregnancy. One of these mothers developed a slight hypertrophy during her second pregnancy and four months after delivery returned to the office with typical symptoms of hyperthyroidism. Her basal metabolism rate at that time was plus 47.8 per cent. Under medical treatment with rest in bed, iodine and sedatives, the rate returned to normal within three months and she later developed symptoms of a mild hypothyroidism.

Another patient who has never had any evidence of thyroid enlargement developed a typical myxedema in 1925 within four months after the birth of her fourth baby. At that time her basal metabolism rate was minus 19.7 per cent and she has required from 3 to 5 gr. of desiccated thyroid per day ever since it was started in November, 1925. All four of her children show evidence of endocrine dysfunction, 2 have enlarged thyroids and 3 of them have definite evidence of hypothyroidism. It is interesting to note that this woman's mother also developed a myxedema at the menopause without any evidence of thyroid hypertrophy and because of this discrepancy in the physical findings suffered from the condition for several years before desiccated thyroid was tried. She has used approximately 5 gr. of desiccated thyroid per

day for more than twenty-three years. If time permitted other cases might be cited to show that myxedema in the mother as well as cretinism in the infant may develop without any previous evidence of thyroid enlargement or disease.

It is evident from observations of patients suffering from thyroid dysfunction that all women living in goiter areas must have careful medication during pregnancy and lactation. The routine administration of small doses of iodine to every pregnant woman is advocated in the belief that it will lessen to a great extent the incidence of congenital goiter, and that it will probably reduce the incidence of cretinism and other evidence of thyroid dysfunction. There is no evidence that the use of small amounts of iodine has been harmful even for the patients with adenomatous goiter or those with a definite hyperthyroidism. However, even if we assume that some slight harmful effect might occasionally be seen in the pregnant woman suffering from a preexisting hyperthyroidism, the iodine still should be administered as a means of protecting the developing fetus.

The regular use of iodized salt has greatly reduced the incidence of congenital goiter in the sections where it has been tried, however, it seems probable that the amount of iodine obtained from it may not be sufficient for the pregnant woman living in a goiter area. It is probably safer to give additional iodine in the form of iodostarine, one tablet every other day, or five drops of the syrup of hydriodic acid every other day. It is also believed that all patients with definite hypothyroidism should have desiccated thyroid throughout the period of pregnancy and lactation as an additional means of protecting the infant. Basal metabolism observations are important, being the only test which enables us to recognize the milder degrees of hypothyroidism. Combined with clinical observations such as the pulse rate, body weight, temperature, bowel movements, perspiration and growth of hair, basal metabolism observations are very important in regulating the dose of desiccated thyroid.

In Pemberton Meadows, B. C., it has been found impossible to rear domestic animals unless iodine is given to the mother during pregnancy and to the young after birth. In the Great Lakes area the incidence of congenital myxedema in domestic animals was high until prophylactic treatment with iodine was introduced. Marine has repeatedly demonstrated the ease with which endemic cretinism in animals may be cured by the administration of iodine or desiccated thyroid if such treatment is started within a few days after birth. His observations indicate that the severest effects of thyroid insufficiency occur during fetal life when irreparable damage may be done to the nervous system if the thyroid insufficiency is great enough. In view of the interrelationship which various observers have shown to exist between the thyroid and the other glands of internal secretion, it is probable that a thyroid insufficiency



of a severe degree in a mother may affect the fetal development of all glands of internal secretion. It has been stated that the pituitary is usually enlarged in patients with simple goiter, cretinism and after thyroidectomy.

Thus far we have emphasized the importance of prophylactic treatment of the thyroid during pregnancy and the years of development. While this is believed to be of paramount importance, the gynecologist is confronted with a variety of problems which are related to the thyroid as well as other glands of internal secretion. It has been recognized for years that a certain type of uterine hemorrhage is associated with hypothyroidism and that it may be corrected by the administration of desiccated thyroid. Litzenberg, Meaker and others have found that thyroid dysfunction may be an important factor in sterility. It is, therefore, evident that in our specialty basal metabolism studies are of great importance and it is believed that they should be obtained more frequently in the study of obstetric and gynecologic patients.

Roth has recently pointed out that the present day clinician guided by a broad survey of metabolic disturbances, their causes and effects, no longer focuses his attention solely on the thyroid or on any other parts of the controlling mechanism of metabolism, but recognizes that the body machine, the rate of activity of which is merely governed by this mechanism, is susceptible to many types of defects or pathologic conditions which are probably more often the initial cause of metabolic morbidity than thyroid, adrenal or pituitary dysfunction. He lists the following conditions in which a basal metabolism study is now recognized as indispensable:

Increased rate in: hyperthyroidism; exophthalmic goiter; thyroiditis; adenoma with hyperthyroidism (toxic adenoma); hyperpituitarism, acromegaly, gigantism; leucemia: lymphatic and myelogenous; anemia, when severe; malignancy, in about 30 per cent of cases; Hodgkin's disease; acidosis, when severe; diabetes, when moderate; arterial hypertension; fever: 7 per cent increase for each degree F. of rise of body temperature (DuBois); convalescence from wasting diseases, and rapid growth.

Decreased rate in: hyperthyroidism; postthyroidectomy; myxedema; cretinism; thyrogenous obesity; hypopituitarism; hypophyseal obesity; hypoadrenalism; Addison's disease in about 15 per cent of cases; undernutrition, starvation; epilepsy; arterial hypotension.

Normal rate in: obesity; endogenous obesity; goiter (without abnormal thyroid function), colloid goiter; adenoma, without hyperthyroidism; heart disease per se; nephritis, without hypertension; pregnancy, in most cases; menstruation (slight increase in the premenstrual period).

It is evident that the interpretation of a basal metabolism may be difficult except in cases where it confirms the clinical findings. An increased rate does not prove that a patient has a hyperthyroidism. A decreased rate is more definite evidence of a thyroid deficiency but desiccated thyroid must always be administered cautiously and in small doses until there is evidence from clinical improvement that the patient really needs this medication.

The obstetrician and the pediatrician are largely responsible for the prevention of thyroid disease. However, the majority of patients are

attended by the family physicians and the specialists must direct them in the prophylactic measures. Marine's contributions in this regard rank among the greatest in the field of preventive medicine.

It also seems probable from a purely theoretical point of view that measures directed toward the development of a normal thyroid may prove to be of value in securing a more normal development of other glands of internal secretion.

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## INTRAUTERINE RADIUM THERAPY AS A CONSERVATIVE METHOD OF TREATMENT\*

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**I**RRADIATION of the uterus may be utilized as either a conservative or radical therapeutic measure: conservative when effectively used in small dosage as a substitute for hysterectomy or other mutilating pelvic operations in the treatment of benign lesions; radical when applied in large dosage to malignant neoplasms, with incidental destruction of function. The elimination of the hazards involved in surgical procedures, with the prospect of equally satisfactory results in properly selected cases, are alluring features of the treatment of nonmalignant conditions with radium. Of course, a knowledge of the physics of radium, the possession of an adequate quantity of the element, familiarity with correct screenage and dosage, accurate diagnosis, and a clear conception of the subsequent histopathologic tissue alterations are requisite for its application. By virtue of his precision in pelvic diagnosis and his operative resources, the gynecologist is particularly well qualified to exercise discriminating judgment, unbiased by over-

TABLE I. BENIGN UTERINE CONDITIONS TREATED WITH RADIUM

Fibromyoma	57
Fibrosis uteri, adenomyosis, and menopausal menorrhagia	27
Hyperplasia of endometrium	11
"Precancerous" endocervicitis	8
Induction of artificial menopause	4
Tuberculosis of uterus	2
Total	109

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enthusiasm on the one hand, and free from the temptation to commit the errors of the inexperienced on the other.

For purposes of review, it seemed desirable to confine the material selected to serve as the basis for this presentation to those patients for whom I can accept personal responsibility and whose follow-up has been supervised by myself, rather than to include all such cases treated in the gynecologic department of the New York Post-Graduate Hospital. From January 1, 1923, to January 1, 1932, I chose intrauterine radium therapy as the preferable method of treatment for 109 patients, whose

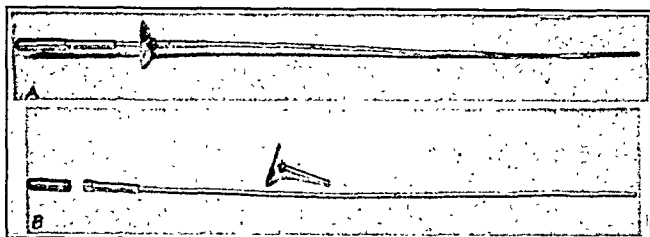


Fig. 1.—Radium applicator. A, assembled, B, disassembled.

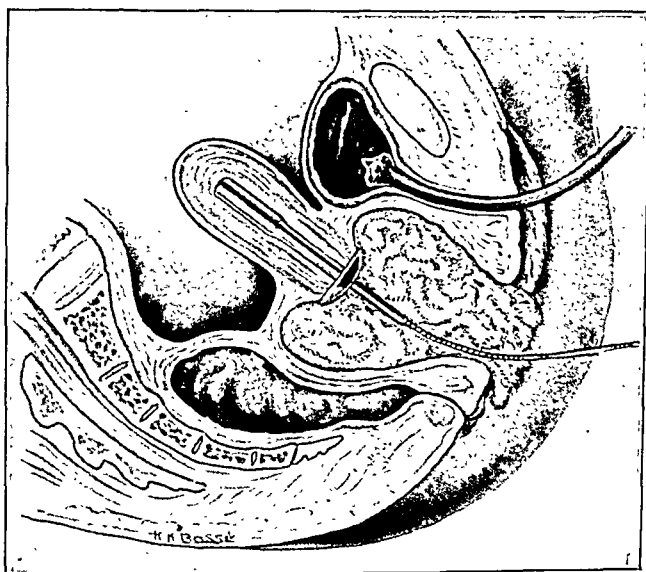


Fig. 2.—Intrauterine immobilization of radium without the use of sutures.

uteri were free from malignancy but would otherwise have required surgery (Table I).

#### TECHNIC

To insure homogeneous dissemination of the gamma rays throughout the uterus, I have designed an intrauterine applicator of nickel silver which conforms to the outline of the endometrial cavity and cervical canal, accommodating two radium tubes in tandem, and attached to a long flexible and malleable shaft. On the shaft there is a sliding aluminum collar with several perforations for drainage, originally devised by Willis, which can be pushed against the cervix after the applicator has been inserted into the uterine cavity (Fig. 1). The chamber for the radium tubes

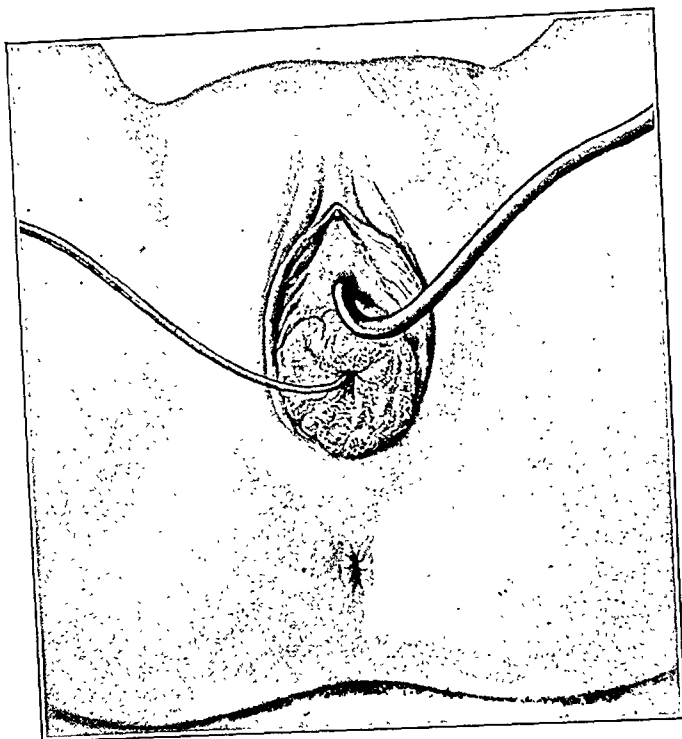


Fig. 3.—The gauze is packed into the vagina both in front and behind the applicator shaft and a Pezzer catheter placed in the bladder.

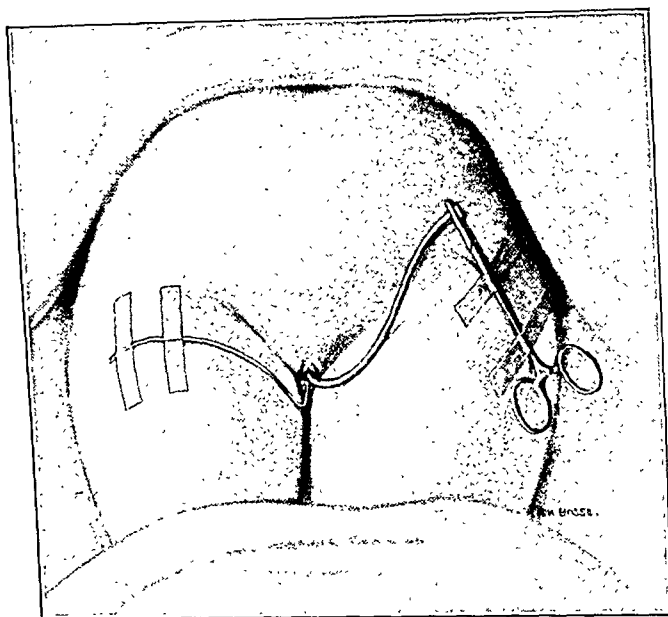


Fig. 4.—Applicator shaft strapped to the patient's thigh, with retention catheter clamped temporarily.

is 60 mm. in length and its walls are 0.5 mm. in thickness. The radium element is enclosed in 1 mm. of brass, so that the total metallic filtration used consists of 1 mm. of brass and 0.5 mm. of nickel silver. A rubber jacket may be slipped over the metal. The aluminum collar, together with tight vaginal packing, maintain the applicator firmly in position without the use of sutures (Fig. 2). The shaft is 300 mm. long, and thus will project sufficiently from the vaginal introitus so that it may be moulded to the contour of the thigh and secured with adhesive plaster (Figs. 3 and 4). Since the proper dosage for individual cases cannot be computed mathematically, it must be estimated by according due attention to the objective to be accomplished, the patient's age, marital state, and childbearing history, the constitutional condition, the size and bulk of the uterus, and the operator's past experience. Before applying radium the uterus should be curetted to determine the character of the endometrium and the outline of the uterine cavity, and especially to detect the presence of small fibromyomatous tumors and unsuspected early fundal carcinoma. Most cases of corporeal cancer are best treated by hysterectomy, and diseased adnexa and ovarian tumors also require extirpation. If there is any uncertainty as to the exact nature of the uterine pathology or any intraperitoneal indication for operative interference, the patient should be treated surgically.

#### FIBROMYOMAS

The 57 cases for radium therapy were selected in conformity with the prevailing opinion that subperitoneal, pedunculated, and degenerating fibroids, as well as those larger than a three months' pregnancy and those causing pressure symptoms, are not adapted to irradiation. Without exception, the tumors so treated were manifested by hemorrhage only. Thirty-nine patients were married, 10 single, and 8 widowed. Seven complained of incidental dysmenorrhea, and 4 had been previously curetted by other physicians without permanent benefit. Paralleling this group of radiated tumors, I did 34 myomectomies and 217

TABLE II. THERAPY SELECTED IN 308 CASES OF FIBROMYOMAS REQUIRING TREATMENT

	NO. OF CASES	PER CENT
Radium	57	18
Myomectomy	34	11
Hysterectomy	217	71
Total	308	100

TABLE III. RADIUM DOSAGE FOR FIBROMYOMAS

AGE OF PATIENT	NUMBER OF CASES	MINIMUM NO. OF MG. HOURS	MAXIMUM NO. OF MG. HOURS	AVERAGE NO. OF MG. HOURS
20 - 30	5	500	600	550
30 - 40	16	500	2400	1021
40 - 50	31	635	1800	1265
50 - 60	5	1200	2400	1635

hysterectomies for fibroids (Table II). It is therefore evident that less than 1 out of every 6, or 18 per cent of white patients with fibroids requiring treatment are suitable candidates for radium therapy. In general, the average dose was slightly increased in direct proportion to the patient's age, but less caution was exercised in cases in which the menopause had already been established or in which its artificial induction would nearly approximate the anticipated time of natural onset (Table III). No single dose larger than 1800 mg. hours was given, but in three cases the initial treatment failed to control the bleeding and a second dose was necessary. Another patient had developed a large bleeding fibroid nine years after an interposition operation and was irradiated to evade a difficult hysterectomy. The radium application alone proved inadequate and was afterward supplemented with x-ray therapy. In two other cases, although the bleeding had been satisfactorily arrested, the tumors progressively enlarged or degenerated during the ensuing two or three years, and were removed surgically. One patient returned after three years of normal menstruation, again complaining of menorrhagia, and was operated upon for an ovarian cyst. The dysmenorrhea was relieved in all patients who had menstrual pain.

#### FIBROSIS UTERI, ADENOMYOSIS, AND MENOPAUSAL MENORRHAGIA

The 27 cases arbitrarily placed in this category included those patients who suffered from inexplicable hemorrhage. Eighteen were married, 2 single, and 7 widowed. They were all free from evidence of constitutional disease, endocrine derangements, and detectable pathologic alterations in the pelvis. In each case the uterus was harder than normal and the curettings revealed nothing of significance. Endometrial gland proliferation into the myometrium is sufficiently common to justify the assumption that adenomyosis may have been responsible for some of these bleedings. One of these patients had been curetted three times by another physician without benefit. Another had been ineffectually treated with x-ray. Radium therapy was not advised for patients in this group until the possibilities of medical treatment had been exhausted. On the whole, they were older than those treated for fibromyomas, and the average radium dose was larger (Table IV). The

TABLE IV. RADIUM DOSAGE FOR FIBROSIS UTERI AND MENOPAUSAL MENORRHAGIA

AGE OF PATIENT	NUMBER OF CASES	MINIMUM NO. OF MG. HOURS	MAXIMUM NO. OF MG. HOURS	AVERAGE NO. OF MG. HOURS
30 - 40	6	500	1200	833
40 - 50	14	450	2200	1216
50 - 60	4	1200	1800	1425
60 - 70	3	1200	1320	1233

largest single dose given to any of these women was 1800 mg. hours, one patient requiring repeated dosage which totaled 2200 mg. hours.

#### HYPERPLASIA OF ENDOMETRIUM

It is noteworthy that 5 of the 11 patients with endometrial glandular hyperplasia had been curetted before coming under observation. In each instance there was transitory cessation of abnormal bleeding, followed by recurrence within a few months. Eight patients were married, 3 were single, and all were less than fifty years of age. Hyperplasia characterized by "Swiss cheese" endometrial glands, or glands tremendously distended with mucus, apparently tends to regeneration after simple curettage, and radium therapy or hysterectomy are necessary for cure. The controlling dosage in these cases was somewhat less than that used for fibroids and fibrosis (Table V).

TABLE V. RADIUM DOSAGE FOR ENDOMETRIAL HYPERPLASIA

AGE OF PATIENT	NUMBER OF CASES	MINIMUM NO. OF MG. HOURS	MAXIMUM NO. OF MG. HOURS	AVERAGE NO. OF MG. HOURS
20 - 30	5	450	1200	675
30 - 40	3	900	1200	1033
40 - 50	3	1200	1400	1266

#### "PRECANCEROUS" ENDOCERVICITIS

While I concur with those who contend that a given cervical lesion either is a cancer or it is not, when the biopsy specimen shows unusual epithelial proliferation or a suggestion of metaplasia, it seems rational to regard the tissue as predisposed to malignancy. In cases of this type, radium was applied as a prophylactic measure, using long platinum-iridium transfixion needles, either alone or with an intracervical applicator. All of these patients were married, none have developed cervical carcinoma up to the present time, and one subsequently was delivered of a healthy baby by cesarean section. Comparatively small doses can be used effectively (Table VI).

TABLE VI. RADIUM DOSAGE FOR "PRECANCEROUS" ENDOCERVICITIS

AGE OF PATIENT	NUMBER OF CASES	MINIMUM NO. OF MG. HOURS	MAXIMUM NO. OF MG. HOURS	AVERAGE NO. OF MG. HOURS
30 - 40	2	300	370	325
40 - 50	2	1200	1920	1560
50 - 60	3	720	1200	973
60 - 70	1	720	720	720

## STERILIZATION

Radium therapy was used to sterilize four women, 1200 mg. hours being given to each one. The first was a patient of thirty-seven with diverticulosis, endocrine derangement, a pronounced neurosis, and moderate menorrhagia. The second was forty years old, suffering from recurrent hyperthyroidism two years after thyroidectomy, who had had an acute exacerbation after a therapeutic abortion two months previously. The third and fourth cases were women of twenty-eight and thirty-four years respectively, both of whom suffered from mitral stenosis and devastating cardiac decompensation during a previous pregnancy and labor, and who emerged as cardiac cripples. Each one had had two therapeutic abortions after the full term delivery, with exaggeration of the decompensation. The cardiac condition precluded tubal resection under general anesthesia and a low systolic blood pressure contraindicated spinal anesthesia.

## TUBERCULOSIS OF THE UTERUS

Radium therapy was utilized in one case of tuberculosis of the endometrium. Both tubes and one ovary had been removed two years before, and the remaining ovary one year previously, by another gynecologist. The patient was only twenty-five years old and complained of constant bleeding. The curettings showed extensive endometrial tuberculosis, and the patient refused a third laparotomy. A single dose of 1200 mg. hours stopped the hemorrhage and the patient has remained well for the past seven years. In another case the radium was used inadvertently, a tuberculous lesion of the cervix being mistaken for a carcinoma. This patient was a single woman of forty-two, and the bleeding continued until a panhysterectomy was done. The diagnostic error was due to the fact that the cervical lesion grossly resembled a basal cell carcinoma although the biopsy specimens revealed nothing but "chronic endocervicitis." Only after the laparotomy was the correct diagnosis made.

## BLEEDING OF PUBERTY AND ADOLESCENCE

This is mentioned simply to emphasize that these apparently idiopathic hemorrhages are nearly always due to endocrine imbalance and derangements of the hematopoietic system. Blood transfusions, organotherapy, calcium, and irradiation of the spleen with small doses of x-ray have arrested the bleeding in all but one of such cases coming under my observation. While radium therapy may be effective, it is unnecessary, unwise, and dangerous. If used at all, it should be applied in small graduated doses as a last resort.

## COMBINED VAGINAL OPERATIONS

All patients in this series were curetted for diagnosis and four required a blood transfusion for severe secondary anemia. In addition,



simple vaginal operations, such as trachelorrhaphy, anterior colporrhaphy, and perineorrhaphy, were performed in many instances with satisfactory results. The radiation evidently has no deleterious influence on wound healing.

#### REPEATED DOSAGE

In three cases of fibromyoma, one of fibrosis uteri, and one of hyperplasia, the primary application failed to control the bleeding within six months, and a second dose was given. The stabilizing end-result of radium therapy in small doses is often delayed for several weeks and a complementary dose is best deferred until four or five months have elapsed.

#### INFLUENCE OF RADIUM THERAPY ON MENSTRUATION

A castration dose should be avoided whenever possible. It seemed particularly important to preserve the menstrual function in 27 women, and the largest single dose given to any of them was 750 mg. hours. Of these, 20 had normal menstrual periods reestablished within six months or less, and 1 after 18 months of amenorrhea. Thus, normal menstruation was successfully preserved in 78 per cent of such cases. On the other hand, an unexpected menopause was precipitated in 6 patients, but these disappointments were somewhat offset by the continuation of menstruation in 6 women who received more than 750 mg. hours.

#### INDUCTION OF ARTIFICIAL MENOPAUSE

The usual climacteric symptoms of flushes, sweats, and psychoneurotic disturbances appeared within six months in 37 of the 109 women treated with radium, but in only 16 were they prolonged or severe. The majority of those who stopped all bleeding did so after one or two periods with either mild or no menopausal symptoms. It would therefore seem that the carefully selected and moderate doses used in this series of cases succeeded in avoiding the abrupt ablation of ovarian function in most instances. I believe that this is due to the fact that the bleeding is checked by fibroblastic proliferation and compression of the blood vessels in the myometrium, rather than because of complete destruction of the secretory activity of the ovary.

#### LEUCORRHEA

Twenty-seven, or about 25 per cent of the patients, reported post-radiation leucorrhea, apparently initiated by the treatment. All were kept comfortable with sodium bicarbonate douches, and the discharge ceased in less than six months in all but 4 cases.

#### EFFECT OF RADIUM THERAPY ON SEXUAL INCLINATIONS

Of the 77 married women treated with radium, 7 reported subsequent frigidity, but in one case this was only temporary. Two complained of vaginal dryness and a burning sensation on coitus, and another of

dyspareunia. On the other hand, 4 who had previously been indifferent experienced a marked and permanent stimulation of their amorous desires. To express it otherwise, there was no disturbance of the patient's domestic happiness in 87 per cent of cases.

#### SUBSEQUENT PREGNANCY

Three patients became pregnant and were delivered of normal babies.

The first was a woman who developed a small fibroid which caused metrorrhagia after fourteen years of sterility. She became pregnant six months after a radium application of 1100 mg. hours. The second was a woman of thirty-one, who had 2 children of seven and four years, and who became pregnant eighteen months after a 500 mg. hour application for a bleeding fibroid. The third was a woman of thirty, who came under observation during her first pregnancy. The cervix bled slightly but persistently from a local lesion, which two eminent pathologists pronounced "pre malignant." She was delivered by cesarean section, and ten days later was given 370 mg. hours with transfixion needles. She became pregnant again two years afterward and was delivered by section a second time. This patient has been watched for six years and the cervix still appears normal. A fourth patient became pregnant three years after radium therapy, but aborted spontaneously.

#### POSTRADIATION COMPLICATIONS

There were no deaths in this group of 109 patients. The single complication noted was an intense uterine colic following a 600 mg. hour dose given for endometrial hyperplasia. This patient had received 300 mg. hours without untoward effects eighteen months prior to the second dose which excited the pain. Intermittent attacks of colic were very distressing for three weeks and then ceased.

#### CONCLUSIONS

1. Radium therapy is applicable as a conservative method of treatment in selected cases of fibromyoma, fibrosis uteri, endometrial hyperplasia, "precancerous" endocervicitis, and tuberculosis of the endometrium after bilateral salpingectomy. It is also serviceable for deliberate sterilization when laparotomy would be unduly hazardous.

2. About 18 per cent of white patients with fibroids requiring treatment are suitable candidates for radium therapy.

3. Larger doses of radium are necessary in cases of fibrosis uteri than for the treatment of fibroids.

4. Radium therapy is an excellent substitute for hysterectomy in cases of endometrial hyperplasia.

5. Transfixion needles, as well as intrauterine applications, are useful in the treatment of "precancerous" endocervicitis.

6. Radium therapy will arrest the bleeding from a tuberculous endometrium after tubal extirpation.

7. Radium therapy has little place in the bleeding of puberty and adolescence.

8. Radium therapy does not interfere with wound healing when vaginal plastic operations are performed simultaneously.

9. Repeated doses are necessary occasionally, but should not be given within six months.

10. The menstrual function will be preserved in 78 per cent of cases when the dose is 750 mg. hours or less.

11. The climacteric symptoms are no more pronounced after induction by radium than when the menopause occurs naturally. In fact, few patients complain of severe annoyance.

12. Radium therapy has a depressing effect on sexual inclinations in about 13 per cent of cases, but sometimes increases them.

13. Patients may bear normal babies after moderate doses of radium.

14. Radium therapy is free from mortality and particularly devoid of morbidity.

580 PARK AVENUE.

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## RESULTS WITH CORDOTOMY FOR RELIEF OF INTRACTABLE PAIN DUE TO CARCINOMA OF THE PELVIC ORGANS\*

FRANCIS C. GRANT, M.D., PHILADELPHIA, PA.

*(From the Neurosurgical Service of the University Hospital)*

PAIN is the most distressing adjunct to disease. Any lesion malignant or benign can be endured until pain develops. But with its first appearance, the situation rapidly becomes intolerable. Tumors in and about the genitourinary tract, especially when malignant, cause pain through infiltration about adjacent nerves or by interference with urinary function. And this pain may be constant day and night wearing down strength and spirit. To relieve this intense, continuous and intractable pain the operation of cordotomy or section of the anterolateral columns of the spinal cord was devised.

In 1904, Spiller<sup>1</sup> confirmed by brilliant clinical observation the theory that pain-conducting fibers from extremities and trunk passed upward to the brain in the spinal cord by way of the anterolateral columns. He proved his contention conclusively in 1912,<sup>2</sup> when at his suggestion, Martin deliberately sectioned the anterolateral spinal tracts with complete abolition of appreciation of painful stimuli in all skin segments below the point of section. Spiller then turned to Frazier,<sup>3</sup> who developed the operative technic for cordotomy and placed the procedure upon a practical basis.

Pain whether unilateral or bilateral in any area below the ensiform can be permanently relieved by cordotomy. No more distressing group of patients is encountered than those doomed by intrapelvic malignancy to die painfully and slowly, riddled with morphine, waiting with as much fortitude as they can muster until death mercifully ends their sufferings. To these unfortunates, cordotomy can offer complete relief.

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\*Read, by invitation, at the Fifty-Seventh Annual Meeting of the American Gynecological Society, May 30 to June 1, 1932, at Quebec, Canada.

Since 1916, 64 cordotomies have been performed upon 61 patients. In 25 cases the procedure was carried out for the relief of pain from pelvic malignancy. Sufficient material, therefore, is at hand to reach a definite conclusion as to the value of this operation.

The results of section of the anterolateral columns can well be illustrated by two cases.

CASE 1.—F. S., female, white, aged thirty-five. Pain persistent and severe running down right leg accompanied by weakness in leg. Panhysterectomy for uterine malignancy two years ago. Radiation treatment to limit of tolerance. Requires between 3 and 5 gr. of morphine a day to keep her comfortable. Left unilateral cordotomy September 10, 1930. No postoperative complications. Pain in right

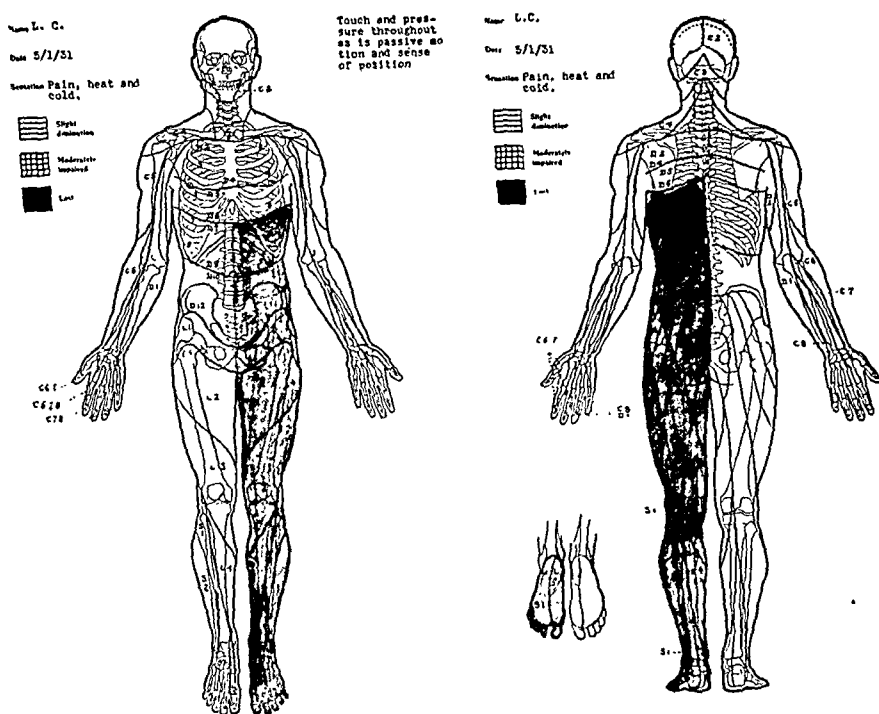


Fig. 1.

leg relieved. Morphine stopped seven days postoperatively. Reported in Follow-Up Clinic, April 11, 1931. At that time, she stated she had no pain in her leg. For two months after operation she had pain in the region of her coccyx and the sole of her right foot itched continuously. These sequelae disappeared and aside from an increase in the weakness of her right leg which was present before operation, her condition is entirely satisfactory. The muscular strength of the left leg is unimpaired.

CASE 2.—L. C., female, white, aged sixty-four. Severe, persistent, intractable pain in the left groin and extending down left leg. Panhysterectomy for cancer of fundus uteri, 1929. Evidence of pelvic metastasis upon vaginal examination. Radiation therapy to point of tolerance. Requires 3 to 4 gr. of morphine a day for relief of pain. Right lateral cordotomy in March, 1931. Complete relief of pain on left side until death in August, 1931. No morphine required after tenth day postoperative. Two weeks before death, pain appeared in the groin on right

side. Made comfortable by  $\frac{1}{2}$  gr. of codeine three times a day. Area of anesthesia is shown in Fig. 1.

These two cases represent clearly the value of cordotomy. Both were relieved of their pain and lived in comfort until the spreading malignant disease ended their lives. Without cordotomy their last days would have been a slow lingering battle with constant pain mingled with shortening periods of ease from ever increasing amounts of morphine.

Cordotomy has three distinct advantages over other methods of relieving pain. First, since in the anterolateral columns of the cord, the pain fibers are compactly collected, a section there produces the largest possible area of anesthesia. Secondly, pain and temperature sensations alone are obliterated without involvement of touch or position sense, and hence the usefulness of the lower limbs is not impaired. Lastly, the operation requires only a small laminectomy and is, therefore, a much less exhausting surgical procedure. But cordotomy has the disadvantage that unless the incision into the cord is accurately placed, the pain may not be completely relieved or the motor pathways may be damaged, resulting in paralysis of the legs and interference with sphincter control.

The technic of cordotomy presents but one difficulty. If the section of the cord is not accurately made the pyramidal tracts may be injured or insufficient pain fibers sectioned to give complete relief. By the use

TABLE I. ANALYSIS OF RESULTS FOLLOWING CORDOTOMY WITH RELIEF OF PAIN

61 Cases	64 Cordotomies
37 Males	24 Females
Bilateral cordotomy	34
Unilateral	30
Completely relieved	47
75 per cent relieved	10
50 per cent relieved	4
Not relieved	3

TABLE II. SUMMARY OF TYPES OF PAINFUL LESIONS REQUIRING CORDOTOMY

Malignancy of the genitourinary tract or genitalia	25
Malignancy of vertebrae	11
G. S. W. spine	4
Sarcoma hip	4
Retroperitoneal sarcoma	2
Painful stump	3
Tabetic crises	2
Osteoarthritis hip	2
Other causes	8

TABLE III. COMPLICATIONS FOLLOWING BILATERAL CORDOTOMY

Vomiting	4
Distention	6
Retention urine	10
Motor weakness	7
Died	6
Meningitis	2
Shock	2
Cachexia	2

of gas oxygen, plus novocaine, it is possible to cut the pain tracts under local anesthesia and to determine with accuracy the level of loss of pain sensation by sensory tests carried out in the operating room. Muscle power in the leg on the side of the section can be tested at the same time. This is a distinct advance in technic that has practically eliminated any damage to motor pathways. Reference to Tables I to IV gives in detail the results with this procedure. In the last 18 cases, there has been no evidence of motor weakness in the lower limbs and no sphincter involvement lasting over three days. In all these cases the relief of pain has been complete.

The point of election for performing cordotomy is the fourth thoracic spinal segment, lying beneath the tip of the second and the body of the third thoracic vertebrae. At this level, the cord is readily accessible. A laminectomy of the second, third, and fourth thoracic spines affords sufficient exposure for a unilateral section, although if both tracts are to be cut, the fifth thoracic spine may be included as a larger exposure is needed.

TABLE IV. COMPLICATIONS FOLLOWING UNILATERAL CORDOTOMY

Vomiting	2
Distention	2
Retention urine	3
Motor weakness	2
Died	4
Cachexia	2
Pneumonia	2

## METHOD

The day before the operation is to be performed, the patient is placed in the prone position and is rehearsed in the tests for pain sensation, especial emphasis being placed upon the differentiation between pain and touch. The surgical procedure consists in the removal of the appropriate lamina under gas oxygen anesthesia and novocaine infiltration. The bony edge of the vertebral canal on the side of the tract section should be cut well back for easier manipulation of the cord. The dura is opened and the point selected at which the anterolateral column is to be incised. A dentate ligament is grasped in a mosquito hemostat and the cord rotated posterolaterally. If a posterior root crosses the field, it is ligated, cut and retracted. The wound edges are now carefully packed with sheets of cottonoid saturated in one-half per cent novocaine. By this means perfect local anesthesia is obtained and the patient's attention is not distracted from the subsequent tests by pain in the operative field. The gas oxygen anesthesia is now stopped. The lower extremity upon the side to which the pain is referred is exposed for the testing of sensation. Time is allowed for the patient to recover entirely from the anesthesia, until replies to tests for pain sensation in the legs and feet are prompt and accurate. The cord is now rotated by traction on the dentate ligament and a very superficial incision made, barely sufficient to cut the pia, from just anterior to the attachment of the dentate forward to the lip of the anterior median fissure. Section of the pain tracts in the cord is not productive of pain stimuli, and may be done upon the conscious patient without causing distress. After this initial incision has been made, loss of pain sensation in the limb is determined. Usually after this first shallow section, pain stimuli about the foot and ankle are

abolished. The incision is now deepened, care being taken never to extend it posteriorly beyond the attachment of the dentate ligament. With each increase in the depth of the section, sensation is tested. The level of anesthesia to pain can be raised from the ankle to the knee, to mid thigh, to Poupart's ligament, to the iliac crest, to the umbilicus and if necessary to the ensiform. But if the pain is referred to the perineum and down the leg, it is not necessary to push the sensory loss above the iliac crest. In this way, just sufficient pain fibers are cut to affect the necessary relief and little or no chance is taken of damaging the pyramidal tract. Furthermore, the muscular power of the leg upon the same side as the incision into the cord may readily be tested to determine whether or not motor pathways are being involved.

If the distribution of the pain indicates the necessity for a bilateral cordotomy, precisely the same procedure is carried out on both sides of the cord. It is important, however, not to cut both anterolateral tracts at the same level. One incision should be two segments above or below the other. After cordotomy has been performed, the wound may be closed under local or gas oxygen as occasion demands.

In deciding upon the necessity for a unilateral or bilateral cordotomy, a careful description of the distribution of the pain is essential. Occasionally patients have the more severe pain on one side with some distress upon the other, often so slight that it is overshadowed by the greater pain and not referred to in their story. But when the major pain is relieved, the minor remains and may later cause unexpected distress. It may be wiser under such circumstances to section both tracts, although the pain seems largely unilateral. If the malignant lesion is rapidly growing, and if the pain while still unilateral involves midline structures both anterolateral tracts should be cut to assure permanent relief. While bilateral cordotomy takes longer to perform than section of but one tract and has twice the chance of complications, nevertheless, in pelvic cancer it is often to be preferred as more certain in its results. In experienced hands, using the technic described, a bilateral cordotomy is but slightly more dangerous than a unilateral section.

Consideration of the 25 cases of cordotomy for pain from malignant disease of the pelvis proves the value of this procedure. In 15 a bilateral cordotomy was performed and in 10 a unilateral. Twenty-one patients were completely relieved, and 4 were considered much improved. Three of these subjects had a unilateral cordotomy with relief of pain, but the opposite side became involved before death occurred. Four patients died following operation. The average duration of life following cordotomy was seven months.

In cases of pelvic malignancy where the disease is sufficiently far advanced to cause pain, the decision for or against cordotomy is one of expediency. The operation is unquestionably sufficiently effective in its results to assure the patient complete relief from pain through the last months of life. And relief by cordotomy means complete relief, not the intermittent comfort afforded by morphine. It is our opinion that it is a merciful act to rid these poor people completely of pain even though it subjects them to major surgery and a week of postoperative

discomfort. Furthermore, as knowledge of the relief afforded by cordotomy is more widely appreciated, this operation will be recommended earlier to prevent pain from becoming the harassing factor it has all too often been allowed to develop into in the past.

## REFERENCES

- (1) *Spiller*: Univ. Pa. Med. Bull. 18: 147, 1905. (2) *Spiller and Martin*: J. A. M. A. 58: 1489, 1912. (3) *Frazier*: Arch. Neurol. and Psych. 4: 137, 1920.

## A NEW AXIS-TRACTION FORCEPS\*

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IT IS with a great deal of reluctance that I presume to present to this Society such an instrument as a new forceps, and for this reason I feel called upon to explain in detail why I should do so. The birth of a new instrument of any kind (if we are completely honest) is brought about through selfishness, by which I mean that it is not through any desire to help the profession, but rather to help ourselves. To illustrate this point, I may be permitted to use my after-coming head forceps as an example. Some years before I had the first design of that instrument made, I had become convinced that the ordinary forceps, when applied to the after-coming head, were clumsy and rather difficult to use, but I had it firmly fixed in my mind that even that awkwardness was preferable to the method of indiscriminate traction on the fetal spine, neck, and shoulders. It seemed to me that I might be able to combine the blades of one instrument with the shank of another and the handle of another, and we could thereby accomplish the desired result. It did and it did not; but changing the instrument here and there gradually brought about some sort of a result, at least insofar as it is moderately satisfactory to me. But even now, after seven years, I am able to see changes that would be a distinct improvement, and the manufacturers are now working on the fifth model, which I trust will be the last. I find it rather amusing to receive the criticisms, which from time to time reach me, as to the manner in which the instrument should be changed. To most of these suggestions I give the only honest answer; which is, that the forceps were designed to suit me, and as they have accomplished that purpose, I can see no reason to change them.

It has been my experience that many of the strongest features of an instrument are either accidental or were designed for some other purpose. As an example of that: In the after-coming head forceps, the first model had a straight shank which I found made too much pressure upon the fetal body, so I had the dropped-shank put in and found that

\*Read at the Fifty-Seventh Annual Meeting of the American Gynecological Society, May 30 to June 1, 1932, at Quebec, Canada.



by so doing I had acquired a sort of axis-traction principle, which was of material benefit. Of course, it would be simpler to say that this was thought out originally that way, but the point is that it was not.

In regard to the axis-traction forceps which I am hereby presenting, I can only ascribe their designing to my lack of ability in using those forceps that are already on the market, and because I rather lean toward simplicity in mechanical devices. The three piece axis-traction forceps, of the various kinds and makes, have been a cause of a marked loss of temper on my part (surprising as that may seem), which was due to the fact that any metallic instrument which is subjected to repeated sterilization must of necessity impair the free action of metal-to-metal joints or metal thread connections as a result of rust, no matter how

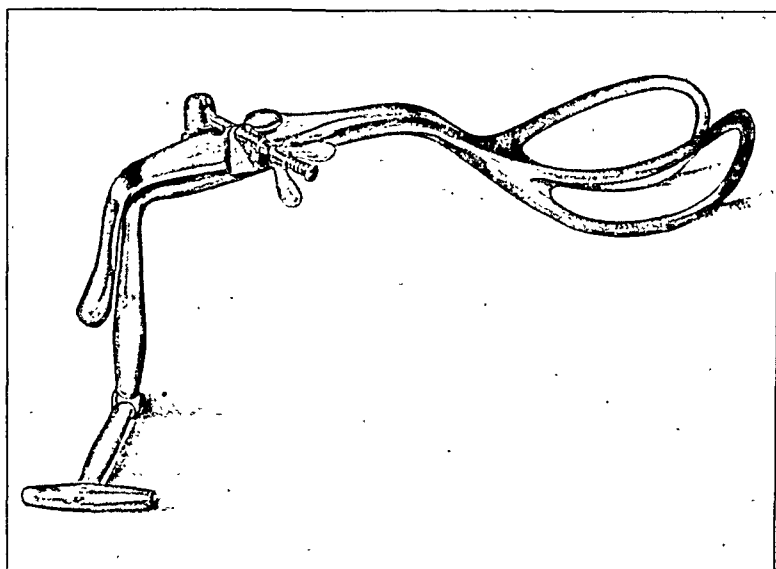


Fig. 1.

careful the nursing staff might be. The result of continually having this difficulty arise was that I acquired the habit of using one of the present-day forceps, namely, the Dewees axis-traction, by allowing the handle to rust tightly on the one blade and applying the blade with the handle already on. This naturally was rather clumsy, and so I had an instrument maker manufacture a pair with the handle and blade in a single piece, having a revolving joint in two places, so that the handle would drop down and not interfere during the application. From that beginning the present instrument was developed, by the slow process of trying it out and changing it here and there as seemed best.

To describe this forceps in detail: The cephalic curve is midway between the exaggerated flat curve of the Tarnier and the marked round curve of the Dewees. The plane of the curve is perpendicular to the plane of the shank at the point where they meet, which is in accordance with the usual construction of forceps and different from the after-coming head forceps. This is done to increase the rigidity of a forceps

in which traction is to be exerted, which in the case of the after-coming head instrument is not necessary, as the latter is designed as a flexor not a tractor. The shank is dropped and somewhat longer than the usual axis-traction but shorter than the after-coming head forceps. The shanks are of the overlapped variety with the French type of lock, with a swivel hinge and thumbscrew lock similar to many others. The extension of the shank of the left blade is bent approximately at right angles to a length at which the line of traction of the blade would pass through. At this point, the handle is put on by means of a swivel joint; the handle being the usual rod running to a larger rod and joined thereto by another swivel joint. The extension of the right blade is bent parallel and slightly beyond the left. This is rather immaterial and could be eliminated, and incidentally probably will be in later models.

This forceps has been used by myself and many others over a considerable period of time and under various conditions. Were I to say that it had never slipped, I would be making a silly misstatement of fact. Frankly, I have yet to see the forceps which fails to slip in my hands; the perfect application of forceps in all cases seems to be beyond the realm of possibility to me. However, when these forceps are put on correctly, there seems to be a rather marked increase in smoothness and power, and this I attribute to two things; namely, the type of cephalic curve and the drop shank. I have tried at various times to use an ordinary forceps and have exerted plenty of power, and have been unable to move the fetal head; upon removal of whatever forceps I might be using and the application of these forceps, I have delivered by the use of two fingers alone. Of course, the argument proposed there against this statement will be that I started the fetal head on its journey, making the work of these forceps much easier. The only answer I can give is that I know this not to be the case. There have been times when we have been confronted with the after-coming head of a breech, failing to engage properly at the brim or failing to come down, where there has been some engagement and the after-coming head forceps have been applied. As has been frequently stated, here and elsewhere, these after-coming head forceps were never designed as tractors and when applied to this type of case have been found to have too much spring and tend to slip. We have removed them, and applied the axis-traction forceps on the after-coming head and delivered a living baby. I merely say this in passing, and shall bring it up later.

The late Dr. J. Whitridge Williams was a firm believer in the obstetrician making himself expert in the use of one kind of forceps, and using that forceps in all kinds of cases. I should not presume in any way to criticize the attitude of Dr. Williams; in fact, I am rather coming a little bit more to that point of view, but there is only one way in which one can find out which type of forceps is particularly adapted to oneself, and that is by trying them all in one's younger days. And I have passed through that phase. At one time or another

er, I have been quite enthusiastic over various types of forceps; I will not mention them by name, nor shall I mention those for which I had no enthusiasm whatever, because I do not care to tread upon anyone's toes. Also, I am fully aware that those forceps which I am incapable of using successfully, in the hands of others give eminently satisfactory results. Of course, the old Simpson forceps is the foundation of all modern forceps, and it is a pleasure to see them used in the hands of such experts as Barton Cooke Hirst, Joseph DeLee, and many others; but, the unfortunate thing is that so many so-called Simpson forceps are as far removed from the real Simpson forceps as the poles. We all know that DeLee, for instance, practically never uses an axis-traction forceps; that he is able by his manipulation to deliver all cases which should have forceps with the ordinary Simpson blades. For his ability to do this, he has my profound respect; I cannot.

To repeat, these forceps were designed for myself. In presenting them, it would have been easy to have worked out the angle of traction and to have made it correspond with the accepted pelvic inclination, but inasmuch as I seem to be an obstetric heretic, I have not done this. Herein lies the heresy: In all of the millions of inhabitants of the world, there are no two people who have faces exactly alike. From my experience with the female pelvis, I should surmise that were we able to calibrate all women's pelves we would not find any two exactly alike, and therefore all we can ever hope to achieve is the mean average, which is what we have tried to do in these forceps without bothering to work out any mathematical angles, etc.

It is a source of sad regret to me, that there is not present to pass judgment upon this instrument my old friend, Dr. John O. Polak, who did me the honor to try these forceps out for two months. I received a letter from him less than one week before his untimely death in which he commented favorably upon this instrument.

A little earlier in this paper, in referring to Dr. Williams and later to Dr. DeLee, I laid stress upon the fact that they both believed in the use of one pair of forceps only. Were I to confine myself to the use of one pair, I would use the instrument herewith presented because it happens to suit me, and frankly, it is almost as easily applied on the after-coming head in a breech as the forceps which were designed for that purpose alone. I have used them with the head in all positions, or rather I should say the occiput, even with the head on the perineum, and have been able to deliver with less maternal injury than I would have caused with any other instrument. Allow me to reiterate, the forceps were designed for myself; anyone is privileged not to like them.

2031 LOCUST STREET.

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*(Abstracts of the discussions on the foregoing, together with the remaining papers presented at this meeting will be published in the November and subsequent issues of the JOURNAL.)*

# Department of Reviews and Abstracts

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CONDUCTED BY HUGO EHRENFEST, M.D., ASSOCIATE EDITOR

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## Selected Abstracts

### Carcinoma

Longo: The Hemoclastic Crisis as a Means of Diagnosis of the Malignant Tumors in the Sexual Sphere of Woman. *Arch. obstet. e ginec.* 17: 1, 1930.

The subcutaneous injection of 1 c.c. of neoplastic vaccine prepared from fresh human malignant tumors has always provoked a marked leucopenia in women bearers of malignant tumors in the genital sphere.

Control investigations in women affected with other gynecologic diseases have constantly given a negative result.

Injection of the same vaccine in normal pregnant women in the second half of gestation has led to marked leucopenia in 40 per cent of the cases.

The author believes that the leucopenia following the injection of neoplastic vaccine may be used as a diagnostic sign. There must be a humoral analogy between pregnancy and organisms affected by malignant neoplastic disease.

SYDNEY S. SCHOCHET.

JULIUS E. LACKNER.

Vogt, E.: The Dangers of Biopsy and Diagnostic Curettement When Carcinoma of the Uterus is Suspected. *Med. Klin.* 27: 1627, 1931.

Biopsy and curettement are minor operations but may at times be dangerous when resorted to in the presence of carcinoma. The chief risks involved are infection and spread of the carcinoma. Many authorities who use radium exclusively for the treatment of cancer of the uterus do not perform biopsies because of these dangers. The infections which follow diagnostic curettage may be local or general and the author cites cases of both kinds. His opinion is that biopsy may be dispensed with in most cases. However, where there is an early cancer, this small operation is necessary in order to be sure of the correct diagnosis.

Many attempts have been made to substitute other measures for biopsy. Hinselmann strongly advocates the use of the colposcope for this purpose. Schiller suggests scraping the epithelium of the portio and also the iodine reaction test. However, the latter test is not infallible.

The technic of biopsy is simple. In order to minimize the dangers however, it is best to use a sharp knife. The neighboring tissue should not be crushed and the wound edges should not be sutured. Bleeding can be stopped by packing the vagina. When performing a curettement, the uterus should not be pulled downward too strongly and the cervical canal should not be dilated more than is absolutely necessary.

The removed pieces of tissue should be examined microscopically without delay and if carcinoma is found, an operation should be performed or radiation therapy instituted immediately. The author emphasizes that the person who is to perform the biopsy or the curettement should be the same one who is to carry out the further treatment. Hence these minor operations should not be performed by general practitioners but by specialists.

Before biopsy or curettage is performed, the vaginal flora should be examined especially for streptococci. If the latter are found they must be removed by treatments before the operation is carried out.

J. P. GREENHILL.

**McNamara, W. L.:** The Histologic Classification of Carcinoma of the Cervix as Regards Ultimate Prognosis. *J. Lab. & Clin. Med.* 15: 976, 1930.

In an attempt to classify malignancy as "high" or "low" from microscopic examinations of biopsy material with special reference to prognosis, the author examined 294 cases of carcinoma of the cervix. The "low" group which included 15 cases is characterized by "pearl" formation and kerato-hyalinization, the cells being uniform in size and non-infiltrating. In the "high" group were found 276 cases. The cells of the cancers in this group are spindle-shaped, closely packed and contain much chromatin. Along with this type of cell is found a round cell with clear cytoplasm and a very highly chromatinized nucleus. This cell never invades tissue. There were three adenocarcinomas in the group but no data with reference to "high" or "low" malignancy can be given with respect to this group. After a three-year period, all cases found within this "high" group were dead. In the "low" group 12 out of 15 were still living at that time, three having died from other causes. Of the three in the adenocarcinoma group all were living after a three year period.

W. B. SERBIN.

**Warren, Shields:** The Grading of Carcinoma of the Cervix Uteri as Checked at Autopsy. *Arch. Path.* 12: 783, 1931.

Warren made a pathologic study in the grading of tumors based on observation at autopsy in 102 cases of carcinoma of the cervix uteri. The power of a tumor to metastasize has been arbitrarily taken as an index of its degree of malignancy. With such a criterion, the personal equation is largely eliminated. A modification of Broder's classification was used, dividing the epidermoid carcinomas on the basis of differentiation of the tumor cells, frequency of mitosis and relation of tumor to stroma into three groups: (I) of low malignancy; (II) of medium and (III) of high malignancy.

A comparison of the distribution of metastases in these 102 cases, shows a close correlation between the degree of malignancy as estimated by histologic grading and the distribution of metastases. Metastasis is uncommon in epidermoid carcinoma, Grade I and visceral involvement is very rare. In epidermoid carcinoma Grade III and in the adeno-acanthomas, metastasis to lymph nodes is the rule, and visceral metastases are common. So far as distribution of metastases is concerned, the degree of malignancy of epidermoid carcinoma, Grade II, and of adenocarcinoma of the cervix is approximately the same. Impairment of the renal function is the most common cause of death in cases of carcinoma of the cervix uteri.

W. B. SERBIN.

**Kamniker, Hellmut:** The Morphological Stage of Maturity of Uterine Carcinoma and Its Meaning in Operative Treatment. *Zentralbl. f. Gynäk.* 56: 457, 1932.

During the years 1921-1925, 304 cases of carcinoma of the cervix were submitted to radical operation. Of this number, 254 cases had complete records and were available for statistics. When these cases were grouped according to their histologic classification it was seen that: of the solid carcinoma simplex, 133 (52 per cent); of the moderately mature epidermoid carcinoma, 73 (56.5 per cent); of the mature epidermoid carcinoma, 16 (50 per cent); and of the adenocarcinoma, 23 (48 per cent) were cured.

Of 49 cases of adenocarcinoma of the uterine body in 40 exact data were available, as follows: of the cases of solid carcinoma simplex, 3 (100 per cent); glandu-

lar carcinoma of low maturity, 18 (55 per cent); glandular carcinoma of medium maturity, 10 (50 per cent); glandular carcinoma of high maturity, 9 (78 per cent) were cured.

The author concludes that it is not possible to place a prognosis on the histologic picture of carcinoma of the cervix treated by radical operation. The clinical and not the histologic findings, as well as the radicalness of the operation decide the prognosis. The same thing holds true for adenocarcinoma of the body of the uterus.

WILLIAM F. MENGERT.

London, B.: **Sarcoma of the Female Genitalia.** *Monatschr. f. Geburtsh. u. Gynäk.* 89: 194, 1931.

During the last eight years at the Breslau Woman's Clinic there were 1,368 cases of carcinoma but only 19 sarcomas (1.4 per cent). In the series of 229 myomas which were removed there were 8 cases of sarcoma, an incidence of 3.4 per cent. Parity plays no rôle in the etiology of sarcoma. The affliction is most common in the fifth and sixth decades of life.

Of the 19 sarcomas in this series 15 involved the uterus and 4 the ovaries. They were of the following types: round cell, spindle cell, giant cell, polymorphous cell, ripe cell and muscle cell.

The notion of older authors that muscle cells become converted into sarcoma cells is false. The term "sarcomatous degeneration" is likewise incorrect. Robert Meyer calls all sarcomas the cells of which have a resemblance to smooth muscle "sarcoma myocellulare."

The only certain way to diagnose a sarcoma is by microscopic examination and in many cases curetted material alone is not sufficient for a diagnosis. This is in contrast to uterine cancer.

Of the 19 sarcomas in the present series, 13 were subjected to operation. The clinical symptoms of sarcoma are not characteristic. In most cases however, there was bleeding, softening of the uterus, rapid growth, pain, bladder and bowel disturbances, loss of weight and cachexia.

There are two methods of treating sarcoma of the genitalia, namely operation and irradiation. The former does not yield good results because most patients die during the first year after operation. In the author's clinic every operable case is operated upon and later irradiated. The inoperable cases are treated with radium and roentgen rays.

J. P. GREENHILL.

Moulouguet, P.: **Metrorrhagia After the Menopause Due to a Tumor or an Ovarian Cyst.** *Bull. de la Soc. d'obst. et de gynec.* 5: 342, 1930.

In a monograph written in 1924, the author reported 50 cases of metrorrhagia which occurred after the menopause and which were caused by a tumor or a cyst of the ovary. Since that time he has operated upon five additional cases. In the service of Hartmann, he found 74 cases of cysts and tumors of the ovary among aged women and in 19 of these cases the tumors were associated with uterine hemorrhage.

The tumors of the ovary may be large and easily recognized or they may be very small and therefore easily overlooked. In 45 of 50 cases the tumor was benign and in only 5 cancer of the ovary was present. The bleeding which accompanies these tumors has a nervous or vascular origin and not an hormonal one. Frequently the uterine mucosa is hyperplastic and not senile in type.

The association of uterine hemorrhage and an ovarian tumor sometimes accompanied by ascites makes one feel that the condition is a malignant one and therefore hopeless. It is a mistake to think so, because an operation may be delayed when in reality operation will produce a complete cure.

J. P. GREENHILL.

Tietze, K., and Mayer, C.: **Bleeding in Women Over 50 Years of Age.** *Monatschr. f. Geburtsh. u. Gynäk.* 88: 185, 1931.

From 1922 to 1930 the writers found at the Kiel clinic 376 cases of uterine bleeding in women past fifty years. These cases were divided into two groups. In the first were those who were either still menstruating or had had their menopause within one year. In the second group were those who had had an amenorrhea for at least one year.

In the first group there were 165 cases and the most important causes of bleeding were carcinoma 24.2 per cent, glandular hyperplasia 26.7 per cent, polyps 17.6 per cent, endometritis 10.3 per cent, myomas 7.9 per cent, and erosions 3 per cent. In the second group there were 211 cases and the most frequent causes of hemorrhage were carcinoma 66.4 per cent, polyps 12.3 per cent, glandular hyperplasia 3.3 per cent, erosions 6.7 per cent, endometritis 1.9 per cent, ovarian carcinoma and glandular hyperplasia 1.9 per cent. In 3.3 per cent of the latter series the diagnosis was not clear.

The above findings agree with those of other authors who made similar studies. Since cancer is so frequently the cause of bleeding in women past the menopause it should be the first thing to think of in these cases. A careful examination should be made not only by bimanual palpation but also by inspection. Furthermore if no definite information is obtained by this means, a biopsy of the cervix or a diagnostic curettement should be done.

J. P. GREENHILL.

Zweifel, E.: **Postclimacteric Metrorrhagia as Symptom of Carcinoma of the Uterus.** *Deutsche med. Wchnschr.* 56: 1388, 1930.

Patients entering the University Clinic in Munich with the complaint of genital bleeding, with an onset later than six months after menopause, were found to have carcinoma in 87 per cent of the examined cases, while patients suffering from metrorrhagia beginning in the first four months after menopause had cancer at the rate of 36 per cent. Thus the extreme importance is demonstrated for early and thorough examination in all cases of uterine bleeding, especially if of postclimacteric occurrence.

G. E. GRUENFELD.

Bends, K.: **Carcinoma of the Cervix After Previous Amputation of the Body of the Uterus.** *Monatschr. f. Geburtsh. u. Gynäk.* 91: 79, 1932.

Among 101 cases of portio and cervix carcinoma, Bends observed three cases of cancer in the cervical stump. In looking over his records of the preceding five years he found four additional cases. These seven cases occurred in a series of 515 cases of cervical cancer. Of the seven previous operations, six were abdominal supra-cervical hysterectomies and one was a vaginal amputation of the body of the uterus. The operations had been performed from eight months to eighteen years before detection of the cancer. The patients complained of hemorrhage and leucorrheal discharge. Two of the cases were operable, three were borderline, and two were inoperable. Six were squamous cell cancers and one was an adenocarcinoma. All of the cases were treated with radium, and after four and six weeks vaginal extirpation was performed on two cases. Of the seven women, two died of cancer, one is alive but incurable, and the remaining four are thus far free from recurrences.

J. P. GREENHILL.

Liepmann, W.: **The Etiology of Carcinoma of the Cervix and Its Relation to the Trauma of Labor.** *Med. Klin.* 27: 846, 1931.

A series of 9,000 cases of cancer of the cervix was studied by Liepmann. He is of the firm belief that this disease particularly affects women who have borne children. He found among his own cases as well as among those reported in the literature that

an average of 90 per cent of all the cases of cervical carcinoma were in women who had had children. This frequency would be still larger if to their number would be added the women who had had abortions and those who had had some manipulation to the cervix in order to prevent conception. All these cases definitely indicate that trauma to the cervix plays an important rôle in the causation of cancer of the cervix. In the far less frequent cases of cancer of the body of the uterus other etiologic factors than injury must be sought.

J. P. GREENHILL.

Keller, R.: *Prophylaxis of Cancer of the Cervix*. Bull. de la Soc. d'obst. et de gynec. 2: 146, 1932.

Keller suggests certain rules for the prevention of cancer of the cervix. The cervix should be inspected for erosions in all cases where there is excessive vaginal discharge after a gonorrheal infection, after labor and where there are irregular scars of the cervix. All erosions or cervical metritis should be treated by cauterization with silver nitrate or the electric cauterium without removal of the cervix. If the erosion persists in spite of this therapy, the cervix should be amputated low down and a careful plastic operation be performed on the external orifice of the cervix to be sure that the mucosa of the cervix and the mucous membrane of the vagina are properly brought together. The excised portion of cervix should be examined microscopically. Each recurrence of erosion should be treated in the same way.

J. P. GREENHILL.

Sampson, J. A.: *Implantation Peritoneal Carcinomatosis of Ovarian Origin*. J. Path. 7: 423, 1931.

The purpose of this paper is to present the evidence that implantation peritoneal carcinomatosis of ovarian origin is nothing more than the result of the repair of injuries to the peritoneum caused by cancer cells which have escaped from ovarian tumors into the peritoneal cavity and lodged on the surface of its serous membranes together with the continued growth of these cells in this situation. The material of Sampson was obtained from 25 cases of peritoneal carcinomatosis associated with ovarian cancer. Twenty of the 25 tumors were either carcinomatous ovarian cysts or cystic adenocarcinomata. Fifteen were bilateral.

The author found that in the repair of the injuries to the peritoneum, the various stages as well as the laws governing the same are similar to those encountered in the repair of tissues injured by foreign bodies, and the taking of skin grafts—namely the healing of wounds. The histologic structure of these implants varies with the reaction of the peritoneal tissues before and after the fixation of the cancer cells and the activity of the latter. As a result cancer becomes embedded in the peritoneal scar, encapsulated on its surface, enmeshed in adhesions, or like the epithelial growth of a successful skin graft spreads over the peritoneum without encapsulation. The malignant cells of these metastatic tumors possess the same potentialities of invasion and dissemination as those of a primary cancer.

J. P. GREENHILL.

Höpper, H.: *Adenofibrosis Retrocervicalis and the Question of the Late Transition to Carcinoma*. Monatschr. f. Geburtsh. u. Gynäk. 87: 536, 1931.

The author describes a case of adenofibrosis retrocervicalis which spread to the parametrium and rectum. Eleven years later this became carcinomatous. The diagnosis was made on the clinical course and the clinical examination. Biopsy of a portion of the growth removed from the posterior vaginal wall verified the diagnosis. The histologic diagnosis was adenocarcinoma. Treatment consisted of radiation of the ovaries and the tumor by means of roentgen rays and mesothorium. The patient has remained well for eight years after this treatment.

J. P. GREENHILL.



# Item

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## American Board of Obstetrics and Gynecology

Attention is called to the following requirements for those who desire to be enrolled in the organization.

### APPLICATION AND CERTIFICATION

Formal application must be made upon a blank which will be supplied by the secretary. A booklet outlining requirements in detail will also be sent on request. This latter describes the necessary credentials and qualifications of the applicant, defines the limitations of the specialty, and gives general information, as well as a list of certificate holders so limiting their work.

Applicants are classified as follows: Group A. Those who have limited their practice to obstetrics and (or) gynecology for a period of ten years or more, having had adequate special training. Group B. Those who have had: 1, at least one year of interne service; 2, five years or more of practice thereafter, including at least three years of special training in obstetrics and (or) gynecology satisfactory to the Board of Directors; 3, and who are now limiting their practice to obstetrics and (or) gynecology. The details of their respective examinations are outlined in the booklet.

The application or examination fee is used entirely for administration expenses. None of the members of the Board receive any compensation for their services. Considerable time and effort is constantly being contributed by the members of the Board, and the assistant examiners.

Older and well established obstetricians and gynecologists will consider it an obligation, it is hoped, to apply for and obtain the certificate in order to promote the efforts of the board by their example and their active participation in its work. It is rapidly coming to be looked upon as a necessity for the younger man who wishes to be established and recognized as a specialist in obstetrics and gynecology.

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### ANNOUNCEMENT OF EXAMINATION

The next written examination of the American Board of Obstetrics and Gynecology will be held on Saturday, October 22, at 2 p. m., in 19 different cities of the United States and Canada (see announcements). In order to reduce traveling expenses for candidates, special arrangements may be made through the Secretary for taking the written examination at any city other than those regularly specified where there is a Diplomate who can be empowered to conduct the examination. This arrangement does not apply to the general, clinical examination to be announced later. For further information address Dr. Paul Titus, Secretary, 1015 Highland Building, Pittsburgh, Pa.

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## Original Communications

### THE MORPHOLOGY OF THE GENITAL EPITHELIA, WITH SPECIAL REFERENCE TO DIFFERENTIATION ANOMALIES\*

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*(From the Gynecological Department of Johns Hopkins Medical School)*

WHILE the genital epithelium presents marked histologic differences in different segments of the genital canal, there is a close kinship between these various epithelia, because of their common derivation from the same mother tissue, the coelomic epithelium. This is in accord with a general law in embryology, as expressed by Fischel,<sup>1</sup> that tissues derived from the same mother tissue are not only closely related, but that they possess a considerable degree of interchangeability. The purpose of this paper is to stress the fact that manifestations of such intermutability of the genital epithelia are not uncommon, and that this must have an influence upon our interpretation of certain pathologic pictures.

The mother tissue of all the genital epithelia is the coelomic epithelium covering the wolffian body. Shortly after the appearance of the primitive sex gland area, when the embryo is in about a 10 mm. stage, there appears just cranial to the sex gland region the infolding of the coelomic epithelium which is to become the muellerian duct. The caudal growth of this duct, and its later partial fusion with the duct of the opposite side to form the genital tract, need not here be redescribed. The point which may be reemphasized, however, is that the various epithelia of the genital canal represent merely different degrees of differentiation of the original coelomic epithelium.

\*Read before the American Gynecological Society, at its Fifty-Seventh Annual Meeting, Quebec, May 30 to June 1, 1932.

NOTE: The Editor accepts no responsibility for the views and statements of authors as published in their "Original Communications."

To put it another way, the coelomic epithelium is, so far as the genital canal is concerned, a "totipotent" one, being capable of forming ovarian, tubal, uterine, cervical or vaginal mucosa. The ovarian epithelium, representing a coelomic epithelium which has, so to speak, used up only a small proportion of its differentiating potency, is likewise capable of much further differentiation, into tubal or uterine epithelium, for example. And so, in diminishing ratio, with the more highly differentiated epithelia, so that, for example, the stratified squamous epithelium of the vagina is a far more fixed one than that seen elsewhere in the genital canal.

The remarkable purposeful adaptation of structure to function is nowhere better illustrated than in this segmental differentiation of the genital epithelium. For example, in a structure like the tube, designed chiefly for transport of the egg from the ovary to the uterus, ciliation is more highly developed than elsewhere in the tract, and the tubal muscle

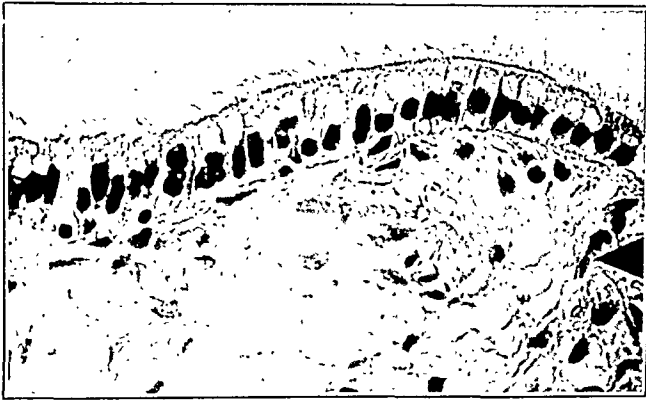


Fig. 1.—Section of fimbria ovarica showing an epithelium consisting entirely of ciliated columnar cells, with no secretory cells whatever, although a few of the latter are at times seen.

is present to assist in propulsion. The mucosa of the fimbria ovarica is covered by cells practically all of which are ciliated, to create the ciliary stream which directs the egg from the ovary into the open mouth of the tube. (Fig. 1.) The endometrium, among other teleologic attributes, possesses an amazing regenerative faculty, so that it can restore itself *ad integrum* almost within a period of hours, and with no scar tissue to tell the tale. Such a property is unique among the tissues of the body. A similar purposefulness may be discerned in the structure of the cervix and of the vagina.

From what was said above, it might be inferred that the direction of the differentiation wave, so to speak, is always from above downward, but this is not necessarily the case. For example, areas of retarded development may often be seen, so that the mucosa at any level may show a degree of differentiation characteristic of a much higher level in the canal, where the differentiating process is not so far advanced. These facts are here stated rather arbitrarily, but I believe they are in con-

formity with facts, aside from possible differences of opinion as to what constitutes a high and what a low degree of differentiation.

We are of course just as ignorant of the forces behind the differentiating processes in the genital tract as we are of similar changes in other systems of the body. Nor can we speak with any knowledge of the cause of localized anomalies of differentiation, such as I expect to discuss in this paper. Whatever the underlying cause may be, it is not easy to understand why these anomalies affect only small areas rather than whole segments which are presumably under the influence of the same cause. The view held by many, and championed especially by Robert Meyer,<sup>2</sup> is that such localized abnormalities of differentiation involve only certain indifferent cells, which have remained slumbering among their more active fellows until some stimulus awakens them to differenti-

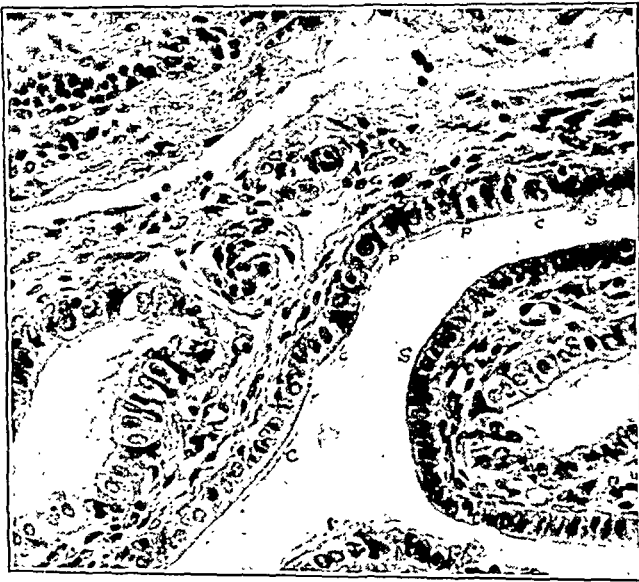


Fig. 2.—Normal postmenstrual tubal epithelium, showing (C) ciliated (nonsecretory), (S) nonciliated (secretory) cells, and (P) peg-cells.

ating activity. Under this impulse they begin to differentiate, reaching stages either behind or ahead of their fellows. There are thus produced areas of over-differentiation or "prosoplasia," on the one hand, or under-differentiation or hypoplasia, on the other. The term hypoplasia in this connection, as used by Meyer, is not a happy one, as it is more commonly applied to gross changes. Perhaps retroplasia would be a better designation.

The theory thus enunciated, based though it is on the assumption of an indifferent type of cell not detectable histologically, appears to be a rational one, and will at least furnish a working basis in the explanation of the histologic abnormalities which furnish the incentive for this paper. Some of these are frequent, some rare, but, in the examination of a large material, I have been struck with the relative frequency of the group as a whole. I shall discuss only the more important among them.

## SOME DIFFERENTIATION ANOMALIES OF TUBAL EPITHELIUM

The tubal epithelium may be considered first of all, because it is a sort of intermediate type between that of the uterus and that of the ovary, and because it, more than any other, presents certain characteristics which appear rather generic of muellerian mucosa. Its normal histology need not be reviewed, except to recall the fact that it is made up of two chief types of cells, one ciliated and nonsecretory, the other nonciliated and secretory. (Fig. 2.) The distribution of these cells varies in different parts of the tube, but they are fairly evenly divided. The striking changes seen in these cells at different phases of the menstrual cycle constitute the tubal analogue of the much more conspicuous menstrual cycle of the endometrium. They have been described in a previous paper by the present author, in collaboration with Everett.<sup>3</sup>



Fig. 3.—Section of tubal ampulla, showing marked inflammatory change, with an endometrium-like picture quite different from that ordinarily seen. The epithelium is of the uterine type, there is a hemorrhagic exudate in the lumen, and the patient has just menstruated. The free bit of tissue in the lumen, apparently thrown off from the tubal surface, looks like desquamated endometrium.

A third type of cell, the so-called peg-cell (*stiftchenzelle*) adds to the distinctiveness of the tubal epithelium (Fig. 2), so that one is accustomed to speak of an epithelium showing these three varieties of cell, and especially the first two in characteristic distribution, as a tubal type of epithelium.

The most interesting anomaly of differentiation encountered in the tube is represented by the finding of definite endometrium in larger or smaller patches, sometimes even encircling small segments of the tube, and often separated from the endometrium of the uterus by broad stretches of normal tube. This abnormality is not common, but I have encountered it a number of times, and a considerable number of such observations are to be found in the literature. Aside from the cases in which perfectly frank endometrium is found, with characteristic epi-

thelium, glands and stroma, there are many instances encountered in which the mucosa represents only an approach to the endometrial type, with gland-like arrangement of the folds and an imperfect stroma.

Of the specimens studied which show this endometrium-like mucosa in the tubes in varying degrees of frankness, two are especially pertinent to the present discussion.

CASE 1.—This patient, a colored woman of twenty-four, had suffered for many months with lower abdominal discomfort and severe dysmenorrhea, and examination revealed bilateral chronic salpingitis, for which double salpingectomy was done on December 19, 1931, just after a menstrual period. The gross examination of the tubes



Fig. 4.—Section of tubal ampulla, showing, above, the endometrial lining, with invasion of the muscular wall (adenomyoma of tube). The latter shows uterine epithelium, glands, and stroma. Below and to left is another smaller invagination, without stroma and with tubal epithelium. A number of similar invaginations are seen in other parts of the section, one being shown under higher power in Fig. 5.

presented no unusual features, both being thick-walled, filled with a brownish exudate, and the fimbriated ends being closed.

Microscopic examination showed a marked degree of chronic inflammation, involving the muscularis as well as the mucosa. The especial point of interest in the latter was the striking resemblance to endometrium seen in many of the sections. (Fig. 3.) The gland-like pattern was quite different from that seen in many cases of follicular salpingitis, and the epithelium lining the glands was of the uterine rather than the tubal type. The stroma showed so much inflammatory infiltration that one could not be sure of a resemblance to endometrial stroma. In some areas there was a picture not unlike that seen in the uterine mucosa in the menstruating stage, and bits of mucosa, apparently thus cast off, could not be distinguished from endometrium. The presence of many red corpuscles in the lumen, with of course also leucocytes, further suggested that a tubal menstruation had actually occurred. This, in view of the histologic appearance of the tubal mucosa, appeared more likely than that the blood and endometrial particles had regurgitated from the uterine cavity.

CASE 2.—The patient, a colored woman of thirty-two, was operated upon January 16, 1932, just at the close of a menstrual period. The operation consisted of supravaginal hysterectomy, double salpingo-oophorectomy and appendectomy for extensive chronic pelvic inflammatory disease, small uterine myomata and chronic appendicitis. Here again the gross examination presented no unusual features except that the exudate within the tubes was described as "chocolate colored and gelatinous." Both tubes showed closed fimbriated extremities.

Microscopically, the chief point of interest was the fact that in the ampullary portion of the tube there was a lining of what was unmistakably endometrium. (Fig. 4.) Sections nearer to the tube showed a characteristically tubal mucosa.

In the annular area of endometrium the tube was moderately distended. The endometrial tissue was in many places flattened out, but in most areas it showed the characteristic endometrial stroma. Here and there the endometrium was heaped up in small polypoid excrescences, showing the characteristic uterine gland pattern. The epithelium here was of the uterine type. In other places there was an adenomyo-

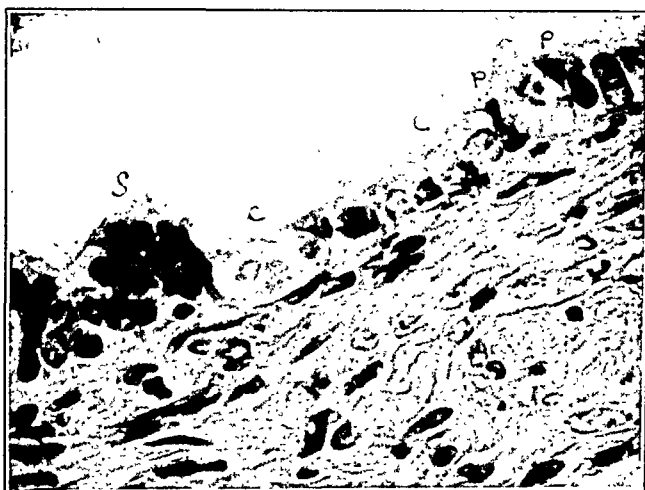


Fig. 5.—High power of wall of a tubal invagination from Case 2, showing characteristic tubal epithelium, without stroma, although derived from the uterine mucosa covering the surface. (C) ciliated cells; (S) secretory cells; (P) peg-cells.

matous invasion of the underlying muscularis, exactly like that seen in uterine adenomyoma.

Some of these invaginations exhibited an abundance of typical endometrial stroma, others showed gland-like patterns without stroma. In some of the latter, although they were obviously offshoots of the endometrium on the surface, the epithelium had again reverted to the tubal variety, with its characteristic cell types. (Fig. 5.) In other words, the normal surface mucosa of the tube had been replaced by endometrium, while in the deeper invaginations, on the other hand, the epithelium had reverted to the tubal type.

The first of these two cases is of interest, first of all, as showing that the abnormal islands of endometrium participate in menstruation and menstrual bleeding. Does not such an occurrence explain the occasional case of hematosalpinx, with perhaps intraabdominal bleeding, in which histologic examination fails to show any evidence of pregnancy? Not much endometrium would be required to produce considerable bleeding, and it could be readily overlooked except through the careful examina-

tion of many sections from all parts of the tube. Such cases have been reported by a number of authors (Meyer,<sup>4</sup> Neumann<sup>5</sup>). In some of these the histories showed that the patient had suffered with lower abdominal cramps at the menstrual periods for some time before coming to operation.

The other possibility which suggests itself in such cases is that the abnormal endometrial areas would strongly predispose to tubal implantation of the egg, as was suggested many years ago by Webster, long before the days of careful routine histologic examinations. This is a logical assumption, although this factor in tubal pregnancy is, from a numerical standpoint, probably a negligible one.

On the other hand, when one considers the interconvertibility, using this term loosely, of tubal epithelium into endometrium, it is not difficult to believe that the former may in some cases possess a physiologic receptiveness to implantation, or that it may, in other words, actually represent an intermediate type of tissue, anatomically tubal but physiologically possessing certain endometrial characteristics. This is perhaps another way of restating the old hypothesis of Webster. In some cases of tubal pregnancy which I have studied, the tubal mucosa immediately adjacent to the implantation area is strongly suggestive of endometrium.

The second case is of even greater interest from the standpoint of the subject of this paper. Here we have to deal with a segment of tube entirely lined by endometrium of a very frank type. The mucosa has, however, penetrated into the underlying muscularis, in exactly the same way as it does into the uterine muscularis in cases of uterine myoma, so that we are justified in applying the designation of adenomyoma to the tubal lesion as well. (Fig. 4.) Of especial interest, however, is the fact that some of the deeper invaginations, obviously continuous as they are with the surface, are lined by an epithelium which is of the characteristic tubal variety, and that the stroma has disappeared. (Fig. 5.)

This case is only one of a considerable group observed in our laboratory in which such intermutability of tubal and endometrial epithelium has been noted. A series of these cases was fully described by Everett<sup>6</sup> in a paper published last year. In this connection also, I have been much interested in the recently published studies of Allen<sup>7</sup> upon the changes observed in the growth of endometrial tissue implanted in the anterior chamber of the eye in rabbits. Of especial pertinence is his statement that "in several instances the proliferated epithelium revealed many characteristics of tubal epithelium; namely, marked ciliation of all cells and the appearance of definite secretion granules."

In the case described above, we have illustrated what I believe to be a surface transformation of tubal mucosa to endometrium, and a reversion in the deeper islands, of endometrium to tubal mucosa. This picture impresses me as a striking illustration of the intermutability of these two tissues. Furthermore it emphasizes the hazard of ascribing a tubal



origin to aberrant mucosa merely because it resembles tubal mucosa morphologically. I shall have occasion, however, to stress this point again later in this paper.

#### SOME DIFFERENTIATION ANOMALIES IN THE OVARY

Of all the genital epithelia the one least removed from the coelomic epithelium, from the standpoint of differentiation, is the germinal epithelium of the ovary. This would at once suggest that this tissue must retain a high degree of differentiating potency, and I believe that this is borne out by the great frequency of differentiation anomalies encountered in the ovary. Under the influence of such stimuli as inflammation, simple morphologic changes in the germinal epithelium are very



Fig. 6.—Low power of the benign serous papillomatous cystadenoma of ovary, from which, at  $\times$ , the high power picture shown in Fig. 7 is taken.

frequent, so that it often becomes very tall and columnar. That it possesses a tendency to push into the ovarian stroma, even in the absence of inflammation, is not surprising in view of the early oophorogenic history of the ovary. For example, the ovaries, especially of women at middle life, frequently exhibit deep invaginations of this tissue, some of which may be cut off from the surface, with the production of the so-called germinal inclusion cysts. In such invaginations and cysts one often finds that the epithelium exhibits tubal characteristics, with ciliated, nonciliated and peg cells in varying proportions. Similar epithelial changes are seen in the surface papillomas not rarely encountered, and sometimes designated as fibroadenoma of the ovary.

From the latter one can, if a large material is examined, detect all grades of transition to the so-called serous papillomatous cystadenoma, so that the germinal epithelium origin of the latter type of ovarian cyst, unlike the pseudomucinous variety, seems to me to be thoroughly estab-

lished. It is therefore of interest to note that in the benign serous cysts the lining epithelium is often of a type exactly resembling the normal epithelium of the tube, with exactly the same types of cells, already described above (Figs. 6 and 7). Indeed, ciliation in such cysts is so common that the group is, by some of the German authors, designated "*cystadenoma serosum cilio-epitheliale*." Such tubal epithelium is of course not constant, and most often is found in patches of irregular size, though in some cysts it may be widely distributed. The point to stress, however, as indicating the intermutability of muellerian epithelium, is that in this ovarian tumor, obviously of germinal epithelium origin, we



Fig. 7.—High power from area X in Fig. 6. The cyst-wall here, and in many other places, is lined by an epithelium which cannot be distinguished from normal tubal epithelium. Note the (C) ciliated and (S) secretory cells, just as in the section of tube shown in Fig. 2. Such findings strongly indicate the muellerian (germinal epithelium) origin of this type of cyst.

see often a type of epithelium indistinguishable from that normally found in the tube.

Of greater interest, however, is the frequent occurrence in the ovary of endometrium indistinguishable from that seen in the uterus. The discussion as to the etiology and histogenesis of ovarian endometriosis has as yet led to no crystallization of opinion on the subject. Only one or two points bearing on this subject need be touched upon here. In going over the material studied for this paper, I have again been struck with the fact that invading germinal epithelium, in cases where surface implantation can apparently be ruled out, often develops typical tubal or endometrial characters. As most of such invaginations are seen on the convex free surface of the ovary, the possible rôle of invading tubal fimbriae does not need to be considered.

Fig. 8, for example, shows such a germinal epithelium invasion of the ovary beneath adhesions on the convex surface of the ovary. Certainly such a picture would be considered in the category of endometriosis, and certainly metaplasia, presumably the result of inflammation, would offer the logical explanation, rather than the implantation theory of Sampson. Such pictures are not rare in the ovaries, and often transitions are seen between such processes as shown in Fig. 8, and the franker types of endometriosis, with hemorrhage and perhaps endometrial cyst formation. Indeed, one finds many variations in the lining epithelium, which may be tubal or uterine in type, may or may not show an ac-

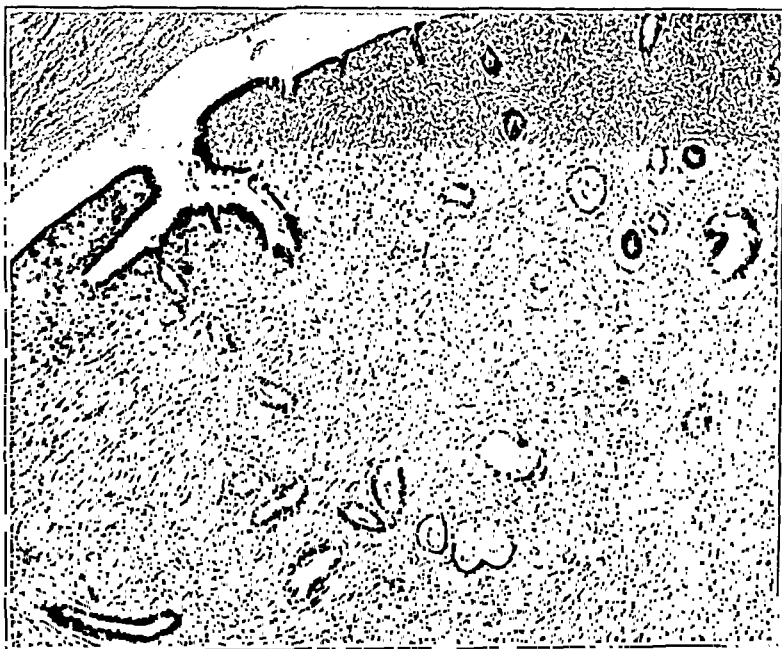


Fig. 8.—Germinal epithelium invasion into ovary, the invading epithelium assuming uterine characteristics, with the formation of many gland-like spaces resembling uterine glands in every way. The endometrium, however, shows no sign of hemorrhagic or functional activity, but this is often true of endometrium in the ovary and elsewhere. Here we are apparently dealing with a metaplasia, presumably of inflammatory origin (note the adhesions on the surface), rather than with implantation. No other endometrium was found in this ovary.

companying stroma, may or may not show hemorrhage and pigmentation. The picture furthermore may vary in different parts of the same lesion.

Another thought-provoking picture is represented in Fig. 9. Here again we have a germinal epithelium invagination, with unmistakable transition from the normal cuboidal epithelium into a type which cannot be distinguished from that normally seen in the tube. Certainly there can be no suspicion here of either implantation or the invasion of tubal fimbriae.

Different constructions can of course be put on such pictures as those I have described in these cases, but I believe them to represent merely

different phases of differentiation. For example, the capacity of endometrium for hemorrhagic or menstrual reaction is by no means invariable in the ovary, any more than it is in the uterus. In the latter, as I shall describe in the next section, we frequently encounter endometrium which, while typical morphologically, is apparently incapable of

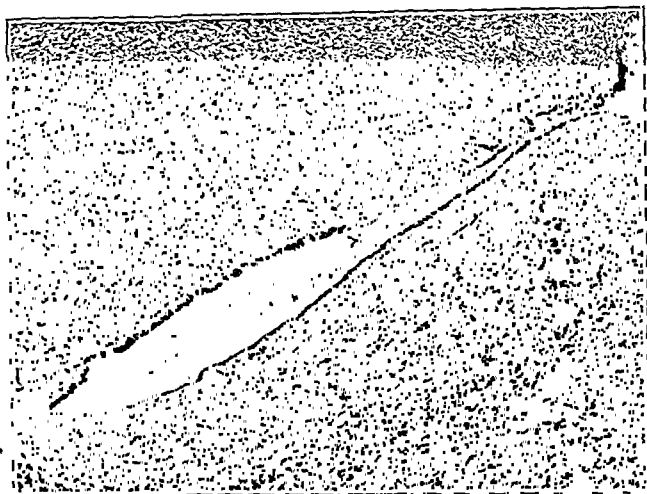


Fig. 9.—A similar cleft in the convex border of the ovary, showing direct transition (X) from the germinal epithelium to one exactly like that of the tube, with both ciliated and secretory cells.

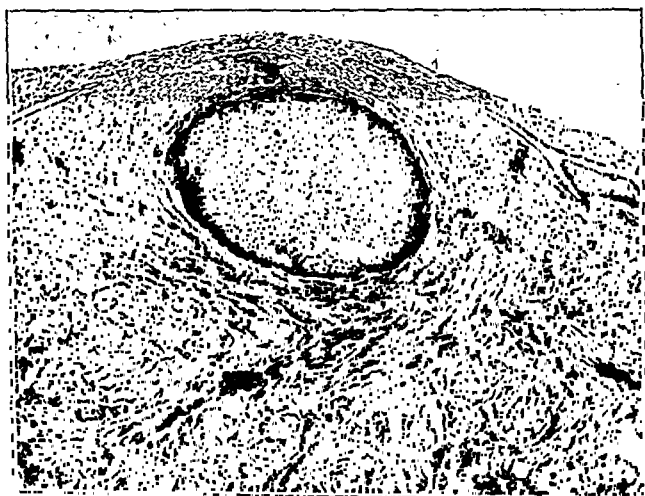


Fig. 10.—Squamous area in broad ligament near hilum of ovary. Such pictures are not rare in the serosa of the tube and at other points in the pelvic peritoneum.

the secretory or hemorrhagic response which one ordinarily associates with the endometrium.

The second point which I should like to stress is that the mere morphology of the lining cells in an area of endometriosis does not warrant drawing any conclusions as to the source of the lesion, or of the supposed "implant," as is sometimes done. For example, it would certainly not be justified to conclude that an endometrial cyst of the ovary is

derived, by implantation or otherwise, from the tubal mucosa merely because its lining epithelium is of tubal type. It would be just as proper to conclude that "tubal" epithelium in a serous cyst of the ovary arises from the tube, or to attribute a tubal origin to the areas of tubal epithelium which, as I shall show, are at times seen in the uterus.

Many other epithelial differentiation anomalies are encountered in the ovary. For example, one occasionally sees on the ovary, or for that matter, on the peritoneum of the tube or broad ligament, sharply marked off "rests" of squamous epithelium. (Fig. 10.) These have generally been assumed to be of embryonic origin, although difficult of explanation. At times, however, one can see a definite transition between peritoneum or germinal epithelium and such areas of squamous epithelium, so that it seems possible that they may in some cases, especially in the



Fig. 11.—Showing apparently a direct metaplasia (X) of peritoneal endothelium, beneath fimbria ovarica, into squamous areas similar to that shown in preceding picture.

presence of inflammation, represent a metaplastic process. It is difficult to reach any other conclusion from such pictures as that shown in Fig. 11.

*Anomalies of Differentiation in the Endometrium.*—Squamous metaplasia of the endometrium is at times encountered, its extreme type being the so-called "ichthyosis uteri," in which the entire uterine cavity is lined by stratified squamous epithelium. There is some difference of opinion as to the explanation of this extreme type, but, at any rate, it illustrates, in an exaggerated way, the possibility of replacement of one type of genital epithelium by another. Smaller, scattered areas of squamous metaplasia are not common in the endometrium, but they are occasionally encountered, perhaps most often in cases of hyperplasia, and in certain cases of adenocarcinoma. In the case of the monkey, Streeter<sup>9</sup> has recently described a remarkable stratification and proliferation, almost epitheliomatous in character, at the two areas in the endome-

trium which are destined to become the sites of the double placenta of that animal.

I have, however, been especially interested in the fact that one often finds in the endometrium areas of epithelium which conform in every way to that seen in the tube. The older textbooks were in the habit of describing the uterine epithelium as of a ciliated columnar type similar to that in the tube. This description is incorrect for various reasons. In the first place, as we have already seen, the tubal epithelium itself is only partly ciliated. Secondly, ciliated cells are exceedingly sparse in the normal endometrium, and are usually not seen at all. Finally, the uterine epithelium differs very definitely from the tubal in its cell types.

The presence or absence of cilia is perhaps best studied by the fresh technic first described by Nylander. In the tube, for example, there is



Fig. 12.—Typical tubal epithelium, with many ciliated cells, in a case of hyperplasia. Cilia are rare in the normal endometrium. With hyperplasia, however, one often finds scattered endometrial areas exactly resembling tubal epithelium, with both, or at times all three of the characteristic tubal cell types.

never any difficulty in demonstrating active and abundant ciliation by pressing out into a thin film under a cover glass, a tiny shaving or scraping of the mucosa, and examining under the higher power, without staining or fixation. By exactly the same technic I have in many cases examined the normal uterine mucosa immediately after either curetting or hysterectomy. Cilia are practically never seen, and this is confirmed by the study of fixed and stained preparations. In rare instances a few scattered ciliated cells may be noted, but they are so rare as to make one feel that they can have no functional value, and that they represent only a vestigial persistence, from a differentiating standpoint, of the ciliated epithelium higher up in the tract. In the tube the presence of cilia can of course be definitely related with function, for they undoubtedly play at least a part in the transport of the germ cells.

In studying the uterine mucosa removed by curetting, I was early

struck by the fact that in cases of hyperplasia of the endometrium ciliated cells, while still sparse, were more often found than in the normal cyclical mucosa. To put it another way, when cilia were found, the mucosa, on subsequent microscopic examination, usually showed hyperplasia, and ciliated cells could often be found in the fixed and stained sections. Of greater interest to me, however, was the fact that in such cases the histologic examination would not infrequently reveal areas in which the epithelium was characteristically tubal rather than uterine in type, an observation which so far as I know, has not been previously made (Figs. 12 and 13).

To appreciate this distinction it must be recalled that in the normally functioning endometrium the gland epithelium, at least, is made up of a uniform type of cell. It is cuboidal or low columnar in the postmen-



Fig. 13.—Another area of tubal epithelium, showing both (C) ciliated and (S) secretory cells, from a case of hyperplasia.

strual phase, becoming taller in the interval stage. With the advent of the secretory phase the gland epithelium of the functionalis becomes lower, takes a pale stain, and later assumes the low, frayed appearance characteristic of the pregravid phase. In contrast to the glandular epithelium, that on the surface remains tall and nonsecretory, and, even in the normal endometrium, it may at times be very reminiscent of the tubal epithelium.

In cases of hyperplasia the glandular epithelium is always of the non-secretory type, and not infrequently in scattered areas one finds an appearance exactly similar to that seen in the tubes. The two chief types of tubal cell, the ciliated and the nonciliated, are clearly distinguishable, while peg-cells are not infrequent. The demonstration of such areas in the stained section obviously explains the not-infrequent finding of cilia in fresh preparations, as previously mentioned. Since hyperplasia is a condition of admittedly endocrine causation, one would naturally think

that such anomalies of differentiation might be explained on this basis. The immediate cause of hyperplasia is believed to be a relative excess of folliculin, with an absence of progestin, while there is evidence to indicate that the underlying disturbance is to be attributed to the anterior hypophysis. It is idle to speculate on the mechanism of these differentiation anomalies except on this broad basis, but that they occur admits of no doubt.

It appears, therefore, that one may find in the endometrium areas of characteristic tubal epithelium, just as characteristic endometrium may be found in the tube or in the ovary. It need scarcely be added that the abnormal areas in the endometrium, like those in the tube, are usually



Fig. 14.—Showing the "stratum reaction" of endometrium, here seen in the pro-gravid phase. Notice the striking difference between the reaction in the middle of the glands (spongiosa) and that in the tips (basalis). The latter is seen best in the basal gland running parallel with the surface, as is so often the case. The epithelium here is nonsecretory, while that in the same gland, nearer to the surface, reacts strikingly to the selective secretory effect of progestin.

small and scattered, and that this change is not of course to be considered as constant in all cases of hyperplasia, for such is certainly not the case. The localized nature of these areas lends support to the view urged by Meyer that only certain persisting cells of indifferent nature retain this capacity for later abnormal differentiation.

There is one other interesting characteristic of uterine epithelium which deserves mention. I refer to the variations in response to physiologic stimuli which are exhibited by the epithelium of the uterine glands, or, for that matter, of any one gland, at different levels of the endometrium. I have called attention to this phenomenon in a previous paper,<sup>10</sup> under the designation of the "stratum reaction" of the endometrium.



If, for example, any one uterine gland in an endometrium of the pro-gravid stage is traced from its mouth down to its tip, which dips into the musculature, a very striking difference of reaction, to what is presumably a uniform physiologic stimulus, may be observed. To take the two extremes, the low mucoid appearance in the spongiosa is in sharp contrast with the sharply stained, nonsecretory epithelium of the tip of the gland in the basal stratum (Fig. 14). Why is the epithelium in one stratum so sensitive to the progestin influence, while that in the basalis is apparently totally unresponsive?

This simple observation, it seems to me, is of profound significance as applied to the whole problem of endocrine physiology. In studying the effects of endocrines we are prone to explain varying effects on the basis of variations in the character and dosage of the hormone administered, without regard to the varying responsiveness of the recipient tissues. In the endometrium, for example, it is quite probable that no amount of progestin would bring about a secretory picture in the basalis, while the functionalis is readily enough influenced.

Innumerable instances of similar variations in tissues presumably of the same histologic structure might be adduced from other organs. Note the varying responsiveness of the ovarian follicles to the same stimulus. For example, in pregnancy, some atretic follicles show extensive theca-lutein change, others none at all. The same is true with hydatidiform mole or chorionepithelioma. For that matter, how can we explain why, of many follicles of about the same histologic phase, only one is responsive in fullest fashion to the cyclic stimuli, so that it alone among all its fellows takes the full charge, reaches full maturation and assumes the ovulatory rôle for that particular cycle? With the same stimulus, why is it that many follicles do not ovulate each month? The answer to these questions is far beyond our ken as yet, but on a broad basis it must be explained by the fact that tissues of the same histologic appearance and derivation differ markedly in their physiologic receptiveness to the same stimuli.

To return to the endometrium, a logical explanation for the stratum reactions would seem to be the age and maturity of the tissues in question. For example, the glands grow in a direction away from their tips, so that the basal endometrium may be assumed to be of a less mature type than that in the upper strata. Perhaps this developmental immaturity is a sufficient explanation of the unresponsiveness to at least the progestin influence, although the cells are responsive to the growth-provoking influence of folliculin.

Whatever the explanation, the fact remains that not all endometrial tissue exhibits the physiologic responses which we ordinarily associate with that tissue. In adenomyoma of the uterus, the aberrant uterine mucosa deep in the uterine wall may, or may not, menstruate. The same is true of the endometrium in uterine polyps. Even more striking are the variations in reaction exhibited by uterine mucosa in the ovary or

elsewhere in the pelvis, in cases of endometriosis. Frequently such ectopic tissue gives abundant evidence of physiologic responsiveness through the presence of menstrual blood, or, for that matter, through the histologic demonstration of the menstrual phases in the endometrium. Perhaps side by side with such areas, however, are others, just as definitely endometrial, which are untouched by the cyclical wave passing over them. I have already, in a previous paragraph, called attention to other variations in this ectopic endometrium, such, for example, as the presence or absence of surrounding endometrial stroma.



Fig. 15.—A common picture in chronic inflammation of the cervix and in cervical polyps, showing replacement of tall cervical epithelium by a stratified squamous epithelium. The possibility and great frequency of this process should always be borne in mind in the differential diagnosis of cancer, although in most cases, the distinction is not difficult.

#### DIFFERENTIATION ANOMALIES IN CERVIX

In this connection the anomaly which at once comes to mind is the frequent replacement of the normal high, cylindrical secreting epithelium of the cervix by a stratified squamous epithelium. This is especially frequent, of course, in connection with chronic inflammation and in cervical polyps (Fig. 15). This so-called "squamous metaplasia," so important in the differential diagnosis of cancer, has been extensively studied by Meyer<sup>11</sup> and others, and I have discussed it at length in one or two previous papers,<sup>12</sup> so that it need not be stressed here. In the presence of chronic inflammation, the invasion of the basal layers of the normal stratified squamous epithelium beneath the cylindrical epithelium, and the lifting and destruction of the latter are often clearly demonstrable, so that we have to do with an invasion rather than with a genuine metaplasia. In many cervical polyps, on the other hand, with little evidence

of inflammation, areas of such squamous type are often found far removed from the normal squamous areas of the cervix, so that here we must have recourse, it seems to me, to Meyer's explanation of metaplasia originating in vestigial cells of indifferent type.

Endometrium may at times be found within the cervix, but more particularly in cases of endometriosis or adenomyoma. So far as I know, however, no one has hitherto described a tubal type of epithelium in the cervix, and yet I believe it occurs. In a number of cases of chronic inflammation of the cervix, I have found that the glands, or, more often, the glandular retention cysts, are lined by an epithelium which is certainly not of the usual cervical type, but which histologically is indistinguishable from that found in the tubes. Such a picture is shown in



Fig. 16.—Section of cervix, showing typical cervical gland epithelium to left, while the lining of the retention cyst, seen on right, is of tubal variety, not in any way like the pressure changes often seen in the usual type of cervical retention cyst.

Fig. 16 taken from a cervical polyp, which externally is covered partly by cylindrical and partly by stratified squamous epithelium. A number of other such instances have been observed, even in the short time since I began the study of this particular question. I believe that intensive study would show them to be fairly frequent.

#### CAUSE OF THESE DIFFERENTIATION ANOMALIES

On the matter of explanation of these differentiation anomalies we can only speculate, chiefly because, as I have already stressed, we know so little of the underlying causes of the normal differentiation of tissues. Meyer's theory of the persistence of *anlagen* of indifferent cells would seem to offer a satisfactory explanation, if we combine with it the view that other factors must be operative to awaken the slumbering differentiating capacities of the indifferent cells. Among the secondary factors to be considered are inflammations, hyperemia, and endocrine influences. In cases of salpingitis, for example, the inflammation may be the factor which incites indifferent tubal cells to differentiate into endometrium,

and this is apparently borne out by the clinical study of such cases, as reported by Meyer, Neumann and others. Hyperemia associated with myomas, retroflexion and other such conditions may perhaps serve in the same way, while the possibility of endocrine participation is suggested, as I have already indicated, by the finding of endometrial "metaplasia" in cases of obvious endocrine disorder. It would, however, be unprofitable to pursue this subject further in the present stage of our knowledge.

## SUMMARY

In this paper I have described the occurrence of certain differentiation anomalies in the epithelium of the various segments of the genital canal. Among them are the occurrence in the tube, of definite endometrial tissue; the occurrence in the ovary of either an endometrial or tubal type of tissue, and even, on the ovarian surface, of stratified squamous areas; the occurrence in the endometrium of either squamous areas or of patches of tubal epithelium; and, finally the frequent presence in the normally columnar cell regions of the cervix of stratified squamous "metaplasia" and the occasional presence of a tubal type of epithelium.

Such anomalies illustrate the tendency toward intermutability of these genital epithelia under certain conditions, a tendency obviously dependent upon their common origin from the same mother tissue, the coelomic epithelium. Cognizance of this fundamental fact must be taken in the interpretation of many pathologic lesions, such as endometriosis. In the latter, direct transformation of germinal epithelium into either a tubal or an endometrial type can be demonstrated histologically, so that it seems unnecessary to invoke the doctrine of implantation in explaining this lesion. All types of differentiation transitions may be seen in ovarian endometriosis, that is, a tubal epithelium with or without stroma, a uterine epithelium with or without glands and with or without stroma, an endometrium with or without physiologic reactivity, with or without hemorrhage.

Among other things, the study of these ovarian epithelia lends strong support to the germinal epithelium origin of serous cystadenomas, for they are often lined by epithelium indistinguishable from that of the tube. The application of such studies to the problem of tubal pregnancy is also discussed in the paper.

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26 EAST PRESTON STREET.

(For discussion, see page 774.)

# THE INFLUENCE OF SEX HORMONES ON THE RETICULO-ENDOTHELIAL CELLS OF THE UTERUS AND A POSSIBLE APPLICATION TO THE TREATMENT OF PELVIC INFLAMMATORY CONDITIONS\*

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THE importance of the reticuloendothelial system for the defense of the body against infection has been repeatedly emphasized during the past few years, and the demonstration of these cells in the human uterus and appendages has drawn attention to the fact that they must play a vital rôle in pelvic inflammation. In a previous communication (Fluhmann<sup>1</sup>) a method was described by which certain phases of this problem could be studied experimentally and the occurrence of large numbers of tissue macrophages in the pregnant rabbit's uterus was demonstrated. The present report deals with an attempt to determine the influence of various hormonal conditions on the presence and activity of these cells in the rabbit's uterus and to discuss the possible application of the results to certain clinical problems.

## EXPERIMENTAL PROCEDURE

The rabbit was chosen as the experimental animal for this work not only because of previous experience but also because it presented two very desirable features. In the first place, since the rabbit does not undergo a spontaneous estrual cycle it was a comparatively easy matter to determine the dominant effect of either ovarian hormone on the uterus at any given time. Secondly, the acute staining with trypan blue called for an animal in which repeated intravenous injections could be given over a period of a few days. The rabbits were purchased on the open market, so that age and previous history were unknown, but an attempt was made not to use does which had had previous litters and to limit them as much as possible to weights varying between 1.5 and 2.5 kilos.

As in the previous study, the macrophages were demonstrated by means of intravital staining. Each rabbit received a total of from 20 to 25 c.c. per kilo body weight, of a one per cent aqueous solution of trypan blue, administered in from 4 to 9 intravenous injections over a period of three days. This procedure resulted in a heavy mortality, but except for a few rabbits in which the macrophages were numerous and easily demonstrated the present report is based on animals surviving and completely stained. They were sacrificed the day after the last injection. The uteri were fixed in formalin, and paraffin sections were made using alum carmine as the counterstain.

The various hormonal conditions studied in these experiments are so generally

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recognized at the present time that a mere mention of them should suffice. The spayed animals of course represent a total absence of all hormonal stimulus to the uterus. The normal unmated rabbit presents a uterus in the estrin phase since the ovaries of these animals contain graafian follicles and no active corpora lutea. The same condition was also reproduced in the spayed rabbit by the administration of urine from pregnant women or of theelin, and it could be intensified in normal animals by giving large doses of theelin. Since no progesterin, the specific hormone of the corpus luteum, was available for this work, the same effect was obtained by inducing a luteinization of the rabbit's ovaries and this in turn produced the progesterin which stimulated the typical progestational proliferation of the uterus. This was accomplished by the intravenous administration of pregnancy urine, but as some criticism might be advanced owing to the fact that estrin is also present in this urine, the same effect was also produced by the use of an estrin-free ovary-stimulating extract made from blood of pregnant women.

The urine was administered intravenously, the usual dose both for specimens from pregnant and nonpregnant women being from 5 to 12 c.c. once or twice daily. The preparation of theelin employed was labelled as containing 50 rat units per cubic centimeter, and in all cases the dose was 0.5 or 1.0 c.c. twice daily. This preparation was given intravenously in a few instances, but intramuscular injections were substituted as this seemed to be more effective.

The method of preparing an "estrin-free ovary-stimulating extract" from the blood of pregnant women is one developed in connection with other studies (Fluhmann<sup>2</sup>) and is known in the laboratory as "Procedure B 118." The blood was obtained by venipuncture and placed in a container with crystals of sodium citrate. This was centrifuged, the cells discarded, and the clear blood plasma extracted five times with ether. Six volumes of 95 per cent ethyl alcohol were then added to the plasma, and the resultant precipitate obtained by centrifugalization was washed twice with ether, dried, ground up in a mortar, and extracted overnight with 20 to 30 c.c. of a sodium acetate-acetic acid buffer having a  $P_H$  of about 4.4. This solution was then centrifuged and treated by adding 10 volumes of 95 per cent alcohol. The resultant precipitate was washed with ether and dried. It was a clear white powder, readily soluble in saline or the buffer solution. This preparation was usually made up for injection so that 1 c.c. of the extract was equivalent to 2.3 c.c. of the original blood plasma.

A total of 89 rabbits survived the various experimental procedures and are available for study. They may be divided into two main groups, namely, (A) animals representing the occurrence of macrophages in the rabbit's uterus under various hormonal conditions, and (B) animals under similar conditions, but in which an injury to the uterus was performed in order to determine the response of macrophages to this stimulus. Each of these two groups is again subdivided into three categories according to the existing hormonal condition of the uterus, namely, (a) postcastration atrophy, (b) estrin phase, and (c) progesterin phase.

A.—1. *Postcastration Atrophy*.—Five spayed rabbits were injected with trypan blue in order to determine the presence of macrophages in the absence of all ovarian stimulation. The castration had been performed from one week to three months prior to the experiment.

2. *Estrin Phase*.—Thirty-one rabbits in which the uterus was under the influence of the ovarian hormone *estrin*, were stained with trypan blue. These, again, are represented by 6 groups:

a. Normal unmated animals (5 rabbits).

b. Normal unmated animals given a series of intravenous injections of urine from nonpregnant women. A total of from 26 to 56 c.c. of urine was given, and they were sacrificed at various times from the fifth to the eleventh day following the first injection (9 rabbits).

c. Normal females given intravenous injections of urine from pregnant women, but in which the progestational proliferation failed to occur and the uterus remained in the estrin phase. Two animals received 20 c.c. of urine and were sacrificed on the fourth day, while the third received 56 c.c. and was autopsied on the tenth day after the first injection (3 rabbits).

d. Spayed rabbits administered theelin. One received 750 rat units intravenously and was sacrificed on the seventh day. One was given 312 units intramuscularly and killed on the tenth day, while two received 500 units and were killed on the sixth and tenth days respectively (4 rabbits).

e. Spayed rabbits given intravenous injections of urine from pregnant women. A total of 40 c.c. was given each animal and they were sacrificed on the eighth day (3 rabbits).

f. Normal animals given theelin. Two animals received 800 and 900 rat units intravenously and were killed on the ninth and eighth days respectively. Two were given 800 units intramuscularly and were sacrificed on the tenth day, two received 400 units and were killed on the fifth day, while one had 850 units and was killed on the ninth day (7 rabbits).

3. *Progestin Phase*.—Nineteen rabbits were used in which a progestational proliferation of the uterus was induced by the administration of urine from pregnant women. The total amount of urine used varied from 26 to 60 c.c. and was given in daily intravenous injections over a period of from three to seven days. The experiments were also completed at various times so that uteri were obtained representing the changes that occurred from the third to the tenth day after the first injection. In four instances the rabbits received 82 c.c. and were sacrificed on the fourteenth day so that the changes present when regression takes place could also be studied.

B.—In the second group of experiments essentially the same conditions prevailed as in the first group, but in addition a traumatic injury to the uterus was performed. This procedure was based on the method of Long and Evans for the production of artificial placentomas in rats and consisted in making a small incision in the lower abdomen of the anesthetized (ether) animal, drawing out one of the uterine horns and inserting a small black silk ligature. The cornu was then dropped back into the pelvis, and the wound was closed by a linen figure-of-eight stitch in the muscle and metal clips for the skin. The operation was generally done the day before the intravital staining was begun so that in all cases the uteri represent the changes found on the fourth or fifth day following the traumatization. A total of 34 rabbits was employed, and this series of experiments may also be subdivided according to the existing hormonal condition, as follows:

1. *Postcastration* (4 rabbits).

2. *Estrin Phase*.—

a. Normal unmated animals (6 rabbits).

b. Animals given pregnancy urine but in which progestational proliferation failed to occur. Four of the rabbits received 12 c.c. of urine, and one 20 c.c. Two were killed on the eighth and one on the ninth day following the first injection (5 rabbits).

c. Normal unmated animals given theelin. One received 400, one 450, and seven 500 units of theelin intramuscularly. Two died on the fourth and seven were sacrificed on the fifth day after the first injection (9 rabbits).

3. *Progestin Phase*.—

a. Animals given pregnancy urine. One rabbit received 12 c.c., five 20 c.c., and one 23 c.c. of urine. One was killed on the seventh, one on the tenth, and the rest on the eighth day after the first injection (7 rabbits).

b. Animals given intravenous injections of an estrin-free ovary-stimulating blood extract (B 118). All received 1 c.c. on one day, and 0.5 c.c. the following morning. They were sacrificed on the seventh day after the first injection (3 rabbits).

## RESULTS

The macrophages are readily recognized by the blue color of the dye particles which they have phagocytized, but since in some animals polymorphonuclear leucocytes also took up the trypan blue, every section was studied under high magnification in order to be assured of the exact nature of the vitally stained cells. Tissue macrophages show considerable individual variation as to size and shape, but generally range from 15 to 30 micra in diameter and present a round or oval outline, although they may be spindle-shaped, elongated, or may branch in one or more directions (Fig. 1). The nucleus is usually round or oval but often kidney-shaped, and is invariably situated at the periphery of the cell.

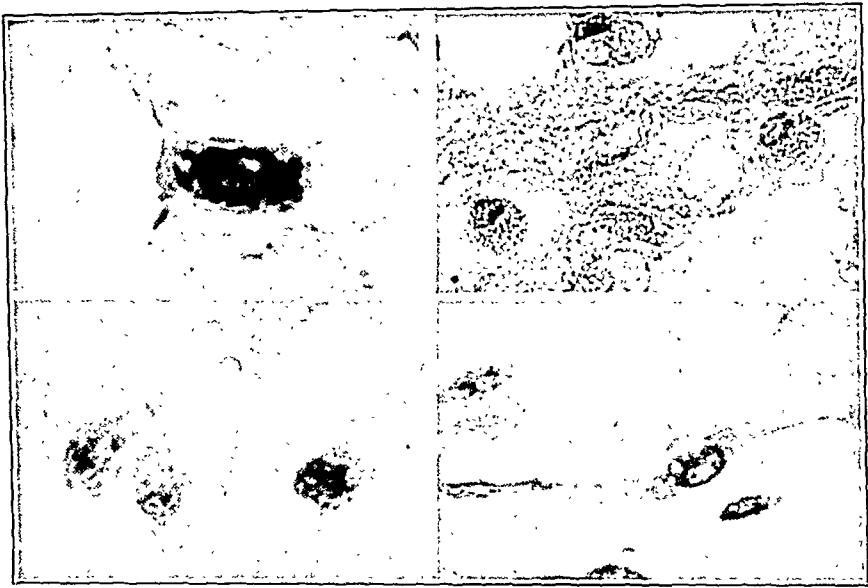


Fig. 1.—Photomicrographs showing various types of macrophages occurring in the wall of the rabbit's uterus (oil immersion magnification).

The cytoplasm is finely granular, vacuolated, and large and small particles of the dye or other phagocytized material are irregularly distributed throughout.

In estimating the intensity of macrophage response in the uteri of the animals, three points have been especially considered. In the first place, the total number of cells present was noted, and in some instances counts were made of the number found in 100 oil immersion fields. Secondly, the distribution of the macrophages proved to be of importance, since usually they are only found in the propria mucosae but under certain conditions they may appear in the lymph spaces of the muscular layers. And thirdly, attention was directed to the intensity with which the cells were stained. On the basis of these three points it was found convenient to grade the reactions in the different specimens into five groups, denoted as 0, +, ++, +++, and ++++.



## GROUP A EXPERIMENTS

1. *Postcastration*.—The uteri of the spayed rabbits had undergone an extensive atrophy of both mucosal and muscular layers (Fig. 2), and a careful search through many sections showed that macrophages were completely absent.

2. *Estrin Phase*.—Since ovulation does not usually occur spontaneously in the rabbit, the ovaries of the normal unmated doe show the presence of mature graafian

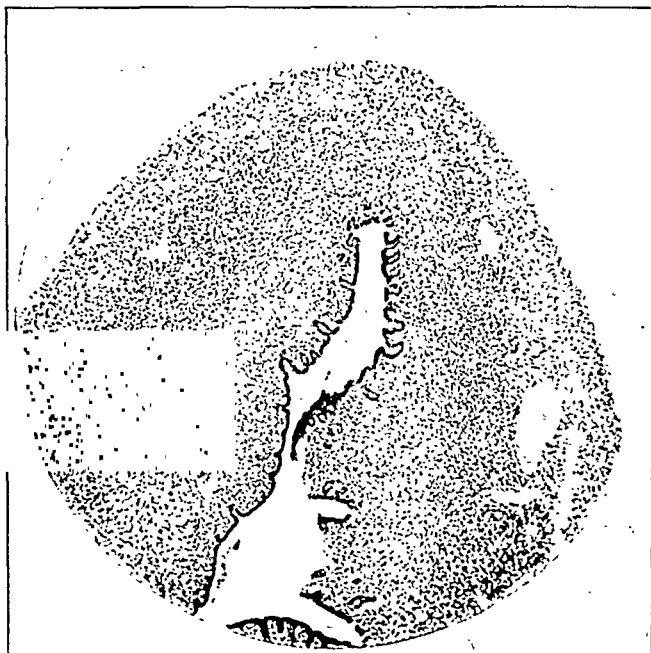


Fig. 2.—Atrophied uterus of a spayed rabbit (low power).

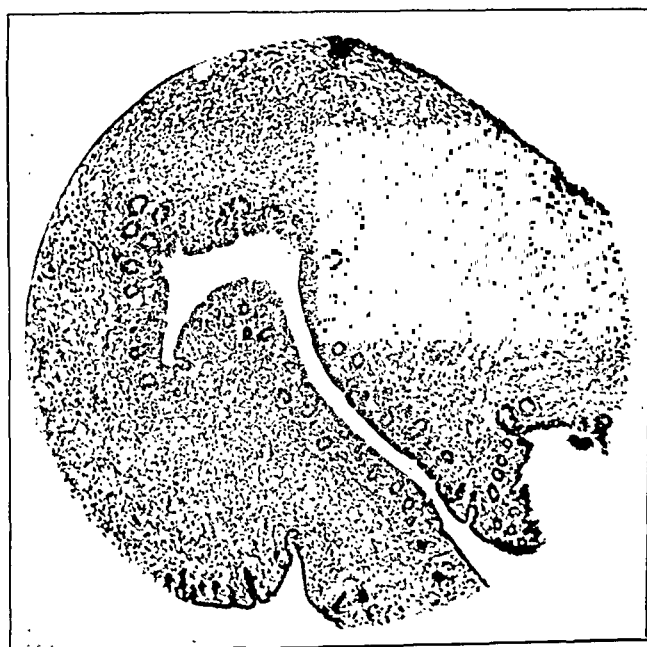


Fig. 3.—Rabbit's uterus in estrin phase (low power).

follicles and the uterus is under the influence of the ovarian follicular hormone (Fig. 3). This condition was represented in this series by three groups of animals, namely, 5 normal females given no treatment except the intravital staining, 9 which received a series of intravenous injections of urine from nonpregnant women, and 3 given injections of pregnancy urine but the progestational proliferation failed to occur and the uterus remained in the estrin phase. The search for macrophages in this group revealed the fact that very few stained cells are usually present, although a slight increase was noted in some of the older heavier animals which had previously had litters. In 7 instances there was a total absence of macrophages (0), in 6 only an occasional cell could be found (+), while in 3 there was a sufficient number present to cite as ++. One large female weighing 3 kilos showed many cells and was estimated as +++ to ++++. The distribution of the cells was

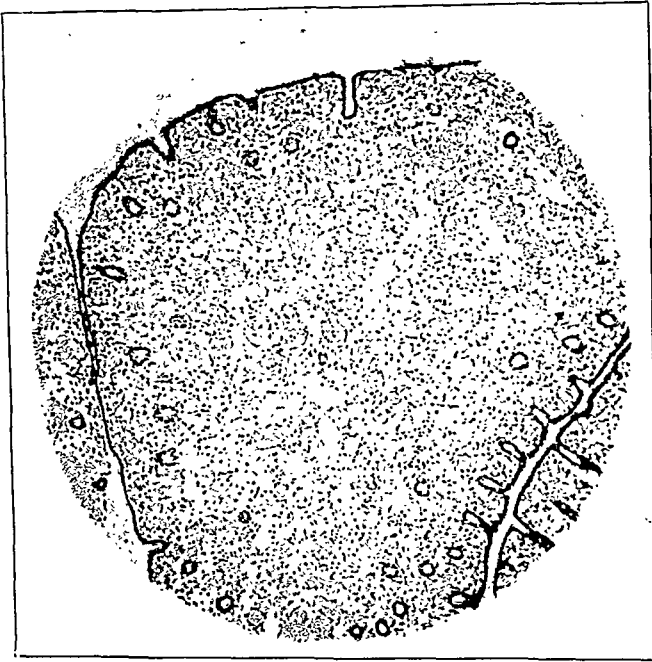


Fig. 4.—Growth of blood vessels in the propria mucosae of the rabbit's uterus induced by the administration of large doses of theelin (low power).

limited, and they were found almost exclusively in the deeper layers of the propria mucosae.

A somewhat different result was noted in the animals administered theelin in spite of the fact that the uterus still had the histologic characteristics of the estrin phase. The uteri of the castrated rabbits which received theelin or pregnancy urine showed that a *restitutio ad integrum* had taken place. The mucosa had developed from a shrunken atrophied structure to its normal state, and associated with this growth large number of macrophages (++ to +++) appeared. This was noted in 5 out of 7 instances. On the other hand, the administration of theelin to normal animals resulted in a marked increase in the number of macrophages (++ to +++) in only 2 instances, while in 3 there was possibly a slight increase (+ to ++), and in 2 there was no noticeable response. Of importance in this group was the evidence of growth in the mucosa, and an accompanying tremendous development of the blood vessels of the propria mucosae (Fig. 4).

3. *Progestin Phase*.—Nineteen specimens are available from animals given injections of urine from pregnant women, which may be considered as essentially

a mixture of estrin and ovary-stimulating hormones (Prolan). The uteri in all cases showed the progestational proliferation of the mucosa with its characteristic treelike development (Fig. 5), which is associated with the formation of corpora lutea in the ovaries and is attributed to the hormone *progestin*. Since the specimens were obtained at various times from three to fourteen days after the first injection of urine they represent various stages of proliferation from the earliest changes to the regression which is apparent on the fourteenth day. In this case, the macrophage response proved inconstant. In 6 instances there was an increase in the number of the cells (+ to +++), in 3 there was a doubtful reaction (+), while in 10 no increase in the number of cells could be demonstrated.

The experiments of this group thus demonstrated the total absence of macrophages in the uteri of spayed animals and their infrequency in normal unmated female rabbits. It was also shown that although a definite macrophage response appeared

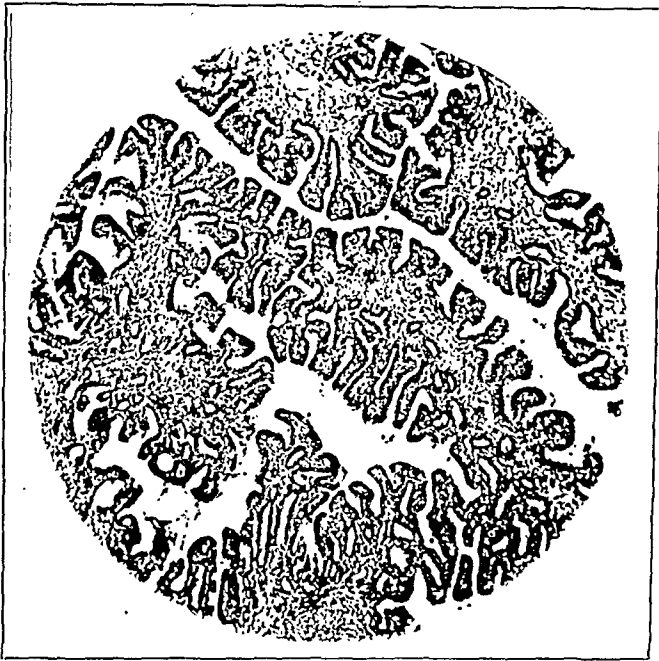


Fig. 5.—Progestational proliferation of rabbit's uterus (low power).

in the atrophied uteri of the castrates when stimulated to growth, it was not possible to consistently effect an increase in the normal animals either by giving large doses of theelin or by inducing the progestational proliferation which resulted from the administration of pregnancy urine.

#### GROUP B EXPERIMENTS

The object of this series was to determine the reaction of the uterus to trauma, and attention was directed to the macrophage response at the site of insertion of the silk ligature, at a distance from this area but in the same horn, and in the opposite untreated uterine cornu.

1. *Postcastration*.—The results of this group were of such uniformity that only 4 animals were used. In all instances a considerable number of well-stained macrophages were observed at the site of injury (+ to +++), but none could be found at any distance from this area either in the same or in the opposite uterine cornu.

2. *Estrin Phase*.—The experiments of this group are represented by 6 normal unmated rabbits and 5 rabbits given pregnancy urine but failing to develop pro-

gestational changes. The findings were essentially the same as in the spayed group, although the macrophage response at the point of injury was more intense. In 8 animals a ++ to +++ reaction was noted at the level of insertion of the ligature, but a ++ was noted only twice at any distance from this area. In 6 instances no cells could be demonstrated in the opposite uterine cornu, a + was found 3 times, a ++ once, and a ++ to +++ reaction once.

A different state of affairs was now to be noted in the group of animals given large doses of theelin before and after the insertion of the silk ligature. The characteristic marked development of blood vessels had taken place, and this could readily be seen grossly at operation when the uterus was found to be of a deep purplish-red color. At the site of injury a local increase of macrophages (+++) was clearly demonstrated as in the previous group, but of especial interest was the widespread reaction present throughout the whole uterus. Sections taken from the injured cornu at a distance from the point of insertion of the ligature and sections taken from the opposite untreated uterine horn revealed a widespread accumulation of deeply staining active tissue macrophages. In 6 cases this was described as ++ and in 3 as ++.

3. *Progestin Phase*.—An effect similar to that produced by the administration of large doses of estrin was found to exist in the group of animals whose uteri were traumatized while they were undergoing progestational proliferation. This was shown in 7 rabbits given pregnancy urine and in 3 which received the extract made from blood of pregnant women. In 7 instances an intense response (+++ to +++) occurred at the site of injury while in 3 it was denoted as ++, but again of importance was the marked reaction found throughout both uterine cornu. The numbers of macrophages and the intensity of the staining in many cases closely simulated the findings during pregnancy. At any point distant from the site of injury in either the treated or the untreated horn of the uterus were found large numbers of macrophages presenting evidence of tremendous activity as shown by the intensity of the staining, their distribution, and the development of new cell forms. In 8 cases this was described as +++ or +++, while it was given as ++ in two instances.

The second group of experiments thus showed that in both spayed and normal animals the insertion of a silk ligature in one of the uterine horns resulted in a fairly intense response with macrophages but this was of a purely local nature and the whole organ did not take part. On the other hand, when the uterus was stimulated to growth by the administration of estrin or underwent the qualitative changes effected by progestin it acquired a tremendous power of responding with macrophages to a traumatic stimulus. This was shown not only in the local accumulation of vitally stained cells at the site of injury but in their increased activity and their presence in exceedingly great numbers throughout the whole organ.

#### ENDOCRINES AND RETICULOENDOTHELIAL SYSTEM

Although only a few attempts have as yet been made to determine if any relationship exists between the various hormones and the reticuloendothelial system, a number of reports suggest that certain endocrinological effects are possibly associated with an increased or decreased activity of the fixed or circulating macrophages. Saxl and Donath<sup>3</sup> found that posterior pituitary gland extract would prevent exudate formation and diminish the production of edema in the experimental conjunctivitis of rabbits. They interpret this result as due to a local depression of the reticuloendothelial cells, although Tainter<sup>4</sup> and others have shown that

both epinephrine and posterior pituitary extract may prevent local edemas and believe that this is due merely to a reduction in the amount of blood flow to the affected area. Goldzieher and Hirschhorn<sup>5</sup> have shown that the storage of trypan blue may be altered by various gland preparations, and somewhat similar conclusions were reached by Leites and Riabow.<sup>6</sup> Mandelstamm<sup>7</sup> demonstrated that epinephrine has a stimulating action on the reticuloendothelial system, as seen in a rapid development of individual cells, increased phagocytosis, and the appearance of new cell-forms. On the other hand, Stephan<sup>8</sup> believes that the suprarenal hormones have an inhibitory influence on the reticuloendothelial system, while Willmore and Douglas<sup>9</sup> described a widespread degeneration of macrophages in a case of suprarenal tumor.

On the basis of the experimental findings of this study, it is impossible to determine the exact rôle of estrin and progesterin in stimulating the macrophage response of the rabbit's uterus. It would seem, however, that estrin is the chief factor concerned and although there is no exact information available as to the mechanism by which this reaction is produced, three possibilities must be considered. In the first place, estrin may have the property of directly stimulating the whole reticuloendothelial system and this conception receives some support from the work of Benda<sup>10</sup> and Lundwall<sup>11</sup> who found evidence of such an increased activity during pregnancy. If this is the case it should be possible to demonstrate a heightened activity of macrophages in other areas than the pelvis, and a number of experiments are at present under way which it is hoped may throw some light on this point.

The second possibility is that estrin may be able to stimulate the production of epinephrine which in turn may be responsible for the intensification of the macrophage response, as suggested by Mandelstamm.<sup>7</sup> However, Dr. M. L. Tainter of the Department of Pharmacology studied this question at my request and was unable to show any marked increased output of epinephrine as demonstrated by the blood pressure record, following the intravenous injection to a cat of as much as 100 rat units of theelin. It would seem very doubtful, therefore, that this explanation is the correct one.

The third possibility was mentioned in the preliminary report of this work (Fluhmann<sup>12</sup>), and would theoretically appear to be the most logical, namely, that the increased macrophage activity is the direct result of the intense tissue growth set up in the uterus by the ovarian hormones. Further credence is given to this conception when one considers the tremendous development of blood vessels which accompanies these changes and the close connection known to exist between the vascular channels and the macrophages. From this standpoint it would be of interest to determine if the macrophage response is increased when the uterus is stimulated to growth by nonspecific substances such as foreign proteins or histamine (Robinson and Zondek<sup>13</sup>).

## DISCUSSION

In considering the possible practical application of this work, it is important to determine the incidence of tissue macrophages in the human pelvic organs, and fortunately there are a number of observations available on this question. The greatest number of these cells is found during pregnancy, when they are seen throughout the uterine wall and in the broad ligament (Hornung,<sup>14</sup> Hofbauer,<sup>15</sup> Motta<sup>16</sup>), while they persist in the myometrium for some time during the early puerperium (Teacher<sup>17</sup>). They may also be readily observed in areas of degeneration in fibromyomata during pregnancy (Fig. 6). Motta<sup>16</sup> has described

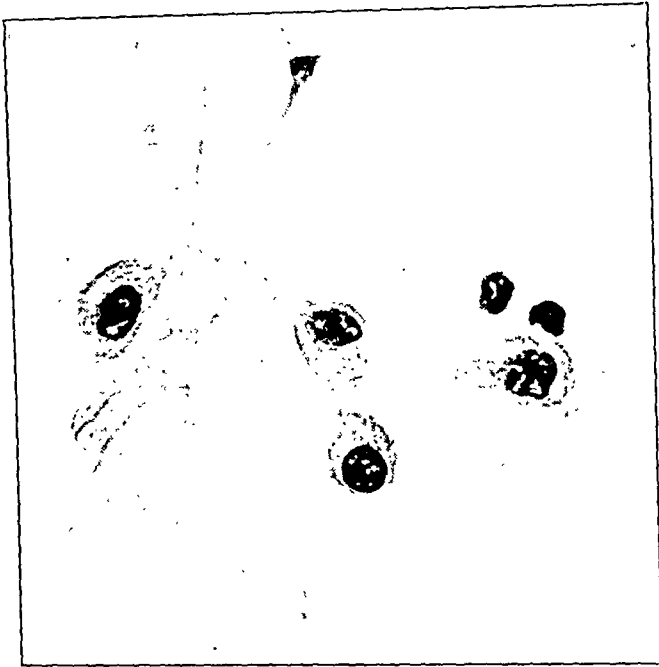


Fig. 6.—Macrophages from a fibromyoma uteri removed during pregnancy (oil immersion magnification).

phagocytic cells consistently present in the connective tissues of the nonpregnant uterus and stated that they greatly increased in number at the time of the menstrual period. Richter<sup>18</sup> studied the presence of reticuloendothelial cells in the female genital organs and believed that they are of an insufficient number to be of practical importance, but it must be noted that his patients were older women varying from forty-nine to sixty-six years of age. The occurrence of tissue macrophages in some cases of salpingitis has been mentioned by Mallory,<sup>19</sup> although no detailed study of this question seems to have been made. It may be said, however, that their implication in these cases is a variable factor, but in some instances they may be demonstrated in large numbers throughout the tubal wall and in the exudate (Fig. 7). Macrophages are also at times seen in the stroma of hyperplastic endometrium, and

a similar, if not identical, type of cell often occurs in the lumina of the endometrial glands (Fluhmann<sup>20</sup>). It may thus be concluded that tissue macrophages *do* occur in the human pelvic organs, and it is also of interest that they have been found chiefly at times when the ovarian hormones exert their greatest influence, while they were few in number in the senile individuals studied by Richter.

The important rôle of the reticuloendothelial system in infection as well as in general and local immunity is now generally recognized, and space does not permit a detailed analysis of this aspect of the problem. The studies of Metschnikoff, Marchand and Maximov are well known,



Fig. 7.—Macrophages in the exudate of a subacute salpingitis (oil immersion magnification).

and a number of valuable reviews have recently been published by Sacks,<sup>21</sup> Jaffé<sup>22, 23</sup> and Gay.<sup>24</sup> It may be said briefly, however, that "the following functions have been attributed to the reticuloendothelial cells in connection with infections: first, the phagocytosis and intracellular destruction of the microorganisms; second, the reception, detoxication and digestion of the waste products that are formed during the process of inflammation, including the toxic substances liberated from the bacteria; third, the absorption of soluble toxins; and fourth, the secretion of the antibodies" (Jaffé<sup>22</sup>).

It is readily seen that any factor which may stimulate the local reaction of reticuloendothelial cells is of vital importance in combating a local or general infection. This has been demonstrated in many ways. Gay and Morrison<sup>25</sup> by stimulating a macrophage response in the pleura

of experimental animals induced a condition which enabled them to survive infections normally rapidly fatal. Nakahara<sup>28</sup> produced a macrophage reaction in the peritoneal cavity of mice and found that as a result they would survive multiples of the fatal doses of streptococci and pneumococci. A closely related phenomenon has been accomplished many times and in various ways in inducing a local skin immunity by Besredka,<sup>27</sup> Mallory and Marble<sup>28</sup> and others. Stuppy, Cannon and Falk<sup>29</sup> found an extensive local accumulation of macrophages in the lung following vaccination against Type I pneumococci. The studies of Louros and Scheyer<sup>30</sup> point to the increased resistance to streptococcus infection resulting from the stimulation of the reticuloendothelial system.

The main interest of these observations as applied to gynecologic problems lies in the fact that certain methods of medical therapy which have been advocated in recent years for pelvic infection have been shown to stimulate the local production of macrophages. The use of colloidal substances, and especially foreign proteins, for the treatment of pelvic inflammatory disease has been recognized for some time and this procedure has been shown by Nissen,<sup>31</sup> Siegmund,<sup>32</sup> Louros and Scheyer<sup>30</sup> and others to produce a stimulation of the reticuloendothelial system. A few years ago, before this Society, Polak<sup>33</sup> recommended the use of mild exposure to roentgen rays as a method of treating similar conditions. Although he attributed the favorable results obtained as due to the temporary amenorrhea which resulted, it is of interest to note that many observers claim that such mild x-ray treatment acts as a stimulant to the local macrophages (Schmidt,<sup>34</sup> Holtermann,<sup>35</sup> Warthin and Case,<sup>36</sup> Schwienhorst,<sup>37</sup> and others).

The marked stimulation of macrophages which has been accomplished in the present study suggests that attention should be directed to the possible use of sex hormones in the treatment of pelvic inflammatory disease. There are no doubt many difficulties to be faced at the present, especially as regards preparations and dosage to be employed, but these should not prove insurmountable. It would seem that large doses of estrin to stimulate a local hyperemia and macrophage reaction without necessitating an ovarian response might prove sufficient, but there is no clear evidence that this is practical with the preparations at present available. On the other hand, Klein,<sup>38</sup> Zondek,<sup>39</sup> and Montag<sup>40</sup> have reported that the use of Prolan in such patients has yielded encouraging results. They have succeeded in inducing a pelvic hyperemia and an accompanying local increase in temperature, while they observed a more rapid disappearance of pain and a shorter period of convalescence. Although an adverse report has been given by Bauer and Lehfelddt,<sup>41</sup> the method certainly deserves a thorough trial. The number of patients treated to date on the Stanford Gynecological Service is too small to draw conclusions from, but it is felt that as an adjunct to the usual con-



servative measures for pelvic inflammatory disease the use of sex hormones may in time prove of considerable value.

#### SUMMARY

A series of experiments were performed to determine the incidence of tissue macrophages in the uterus of the rabbit, as well as the macrophage response following trauma, under various hormonal conditions.

The uterus of the normal female rabbit was found to contain only a few macrophages scattered throughout the propria mucosae, while they were totally absent in the atrophied uterus of spayed animals. The injection of large doses of estrin or the induction of progestational proliferation of the rabbit's uterus by the administration of urine from pregnant women resulted in an increase in the number of macrophages in less than 50 per cent of the cases. However, the growth of the spayed rabbit's uterus which resulted from estrin stimulation was associated with the appearance of large numbers of macrophages.

The traumatization of one horn of the uterus resulted in the appearance of many macrophages at the site of injury in all animals, but in the normal doe or in the spayed animal this was of a purely local nature. In the rabbits given large doses of theelin or in which a progestational proliferation had been induced, the response was tremendously increased and was apparent not only at the site of injury but throughout the whole uterus.

It may thus be said that when the rabbit's uterus undergoes the tissue differentiation and vascular changes brought about by the ovarian hormones estrin and progesterin, it acquires the power of responding much more actively with macrophages to traumatic stimuli.

The possibility of employing sex hormones in the treatment of pelvic inflammatory conditions is discussed.

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## INCREASE OF GUANIDINE COMPOUNDS IN ECLAMPSIA: AN EXPERIMENTAL STUDY\*

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ROUTINE blood chemistry studies in preeclampsia and eclampsia have been disappointing, but biochemistry as a special field for the investigation of these conditions still offers immeasurable possibilities.

Studies of the behavior of the blood sugar in preeclampsia and eclampsia with which our group has been concerned<sup>1, 2, 3, 4, 5</sup> indicate that these toxemias have a hypoglycemic basis. We have demonstrated wide fluctuations in blood sugar during eclampsia with sudden and sharp falls in the sugar preceding the convulsions, as well as a general trend toward hypoglycemic values. These findings have recently been confirmed by others.<sup>6, 7, 8</sup>

We are now convinced that a disturbance in carbohydrate metabolism is common to all types of pregnancy toxemia, and originally believed that the basis for this was a simple deprivation or deficiency of carbohydrates, mainly dietetic in origin. It seems apparent, however, that there must be some added element which causes either a direct loss of body glycogen or else a disturbance in the normal glycogenic function of the liver or both, especially if the disturbance is to develop into such a violent clinical upheaval as an attack of eclampsia.

In a search for possible causes of such unusual metabolic findings as these blood sugar fluctuations which we have described in eclampsia Dr. H. D. Lightbody, formerly director of this laboratory, attracted our attention to the recent work of Minot and Cutler<sup>8, 9</sup> on the association between liver injury and increase of guanidine in the blood, as well as the fact of the hypoglycemia produced by toxic doses of

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guanidine and its compounds.<sup>10, 11, 12, 13, 14, 15</sup> This latter phenomenon has been extensively studied in connection with the use of synthalin, a complex guanidine derivative originally developed for use in reducing blood sugar in diabetes but now abandoned because of its toxicity.

The toxic effects of this and other guanidine compounds have been investigated experimentally as well as clinically, and several interesting facts develop from this work. It is significant to discover that by overdosage with certain guanidine compounds one may reproduce in animals practically all of the clinical features of eclampsia in the human being. These include disturbed carbohydrate metabolism, fluctuations in blood sugar, increase in blood uric acid, amino acid and lactic acid, increase in blood pressure, edema, albuminuria, muscular tremor, and a series of convulsions ending in death.

#### HYPERGUANIDINEMIA AND HYPOGLYCEMIA

Guanidine poisoning promptly produces a hypoglycemia, and Minot<sup>15</sup> has shown that the mechanism by which this occurs is a simple one. It is, namely, that this intoxication seems to interfere with oxidative processes in the tissues resulting in an accumulation of lactic acid, with a secondary rise in its concentration in the blood whereupon "much lactic acid is excreted in the urine. This accumulation and loss of lactic acid represents a serious drain on the carbohydrate reserves" resulting in secondary hypoglycemia. She also advances evidence to show that accumulation of guanidine interferes with normal glycogenolytic functions of the liver and with calcium metabolism.

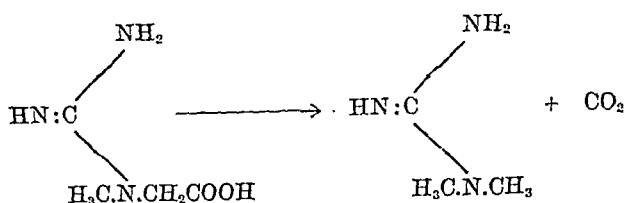
Minot and Cutler<sup>8</sup> report an increase in guanidine-like substance in acute experimental and clinical liver injury, and in eclampsia, all three being accompanied by the characteristic hypoglycemia. We have corroborated their findings in a small number of cases of preeclampsia as well as in hyperemesis. A normal average of presumable blood guanidine, according to Pffner and Myers<sup>16</sup> is 0.23 mg. per 100 c.c. of blood, whereas in our hyperemesis cases we found from 0.50 to 0.60 mg. and in preeclampsia from 0.65 to 1.0 mg. Minot and Cutler found values between 0.50 and 0.85 mg. in preeclampsia and eclampsia. The terms "presumable guanidine" and "guanidine-like" substances are explained in the next paragraphs.

#### SOURCES OF GUANIDINE AND ITS CHEMICAL IDENTIFICATION

Nothing definite is known about guanidine metabolism in the body. It is believed that one source of the guanidine grouping in the system may be the purine guanine, thus linking it with purine metabolism as an end-product. This would be consistent with the clinical view that excessive meat consumption is harmful in pregnancy toxemias, but there is not the slightest experimental evidence to establish this.

Another reasonable but unconfirmed belief of one of us (Messer) is that creatine is in some way responsible for guanidine. By reduction and demethylation creatine might form guanidine. By reduction alone methyl guanidine might be formed. Dimethyl guanidine, which we have

found experimentally to be the most toxic of these combinations, could be obtained from creatine by the mere elimination of one molecule of  $\text{CO}_2$  as follows:



The Tiegs-Marston reaction for the guanidines, the basis of all contemporary methods for their estimation, is not specific, developing color not only with guanidine, methyl guanidine, and dimethyl guanidine, but also with creatine, creatinine, urea, arginine, histidine, cysteine, adrenaline, and some of the alkaloids.<sup>16</sup> The various analytical methods include procedures attempting to separate the guanidines from the other chromogens, with varying success. It will be seen that in the absence of dependable data on the direct isolation of guanidine bodies from the blood, our evidence for their presence there is indirect.

Nevertheless the method devised by Piffner and Myers<sup>16</sup> for estimation of guanidine compounds in the blood, which was the method used by us, minimizes the colorimetric interference of these other substances. For example, creatine which may be present and could give the same reaction is condensed by the Piffner-Myers technic into creatinine. This eliminates its interference because the colorimetric reaction of this substance develops so much more slowly than that of guanidine that readings may be made for the latter before the other appears.

Minot and Cutler<sup>8</sup> used the method of Major and Weber for their estimations. This provides for a correction for interference due to creatine.

While the objection is therefore to be offered to the finding of increased guanidine-like substances in pregnancy toxemia, that estimations of blood-guanidine are not specifically accurate, the significant fact remains that the experimental administration of guanidine compounds to animals produces a train of symptoms closely resembling clinical eclampsia.

#### GUANIDINE ACCUMULATION AND LIVER NECROSIS

In the association of liver damage with guanidine accumulation, which factor is the cause and which is the effect has not finally been established.

Minot and Cutler believe that the increase in guanidine results from the liver injury, being formed in the process of necrosis of liver tissue, whereas Elkourie and Larson<sup>27</sup> state that guanidine intoxication causes liver necrosis. Others<sup>18, 20, 22</sup> have made similar observations but in all except one of these recorded instances the experimental animals were killed by single lethal doses of some guanidine compound, a procedure which does not imitate the slower and more gradual accumulation of toxins which must take place in preeclampsia and eclampsia. Furthermore,

it is suggested that these investigations were controlled insufficiently to be conclusive.

It seemed a simple matter to obtain evidence for or against the idea that excessive guanidine formation could precede the liver destruction, granting the obvious fact that more would form and accumulate as a direct result of this necrosis.

To discover the correct sequence of events we determined to treat normal, healthy rats with sublethal doses of guanidine until an acute or profound toxemia was produced. Some of these were to be allowed to die while others were to be killed. Histologic examinations of the liver and kidneys of all of them were to be conducted, and if pathologic changes, such as liver degeneration or necrosis, were found in properly controlled animals it should then be apparent that this was a result of the guanidine poisoning.

Extensive investigations of the biochemical and clinical effects of guanidine poisoning have been made by others and will be briefly outlined for the sake of reference.

#### CLINICAL AND BIOCHEMICAL EFFECTS OF GUANIDINE ADMINISTRATION AND THEIR RESEMBLANCE TO CERTAIN CHARACTERISTICS OF ECLAMPSIA

Before proceeding to a description of the technical details of our experiments and findings, it is desirable to review briefly the clinical and biochemical results of guanidine poisoning previously referred to, especially because of their resemblance to the symptoms of preeclampsia and eclampsia.

*I. Disturbance in Carbohydrate Metabolism.*—Minot's explanation of the occurrence of the hypoglycemia from guanidine intoxication has been outlined above. She further reports that rats so poisoned develop one of two types of abnormality of carbohydrate metabolism; either a hypoglycemia with a liver progressively depleted of its glycogen, or one without such depletion. In the latter instance she believes that guanidine accumulation interferes with normal glycogenolysis thus being an additional factor in the loss of carbohydrates through lactic acid formation and its renal spill, without compensation in these instances from the liver stores.

*II. Fluctuations in Blood Sugar.*—The hypoglycemia following guanidine administration described by Watanabe in 1916<sup>10</sup> is such a characteristic symptom that Colip<sup>21</sup> later considered insulin to be a guanidine derivative, while Frank, Nothmann, and Wagner<sup>22</sup> synthesized "synthalin" (diguanidino-decamethylene) in an effort to provide an insulin substitute for oral administration. These latter authors in 1926 demonstrated blood sugar fluctuations and concomitant convulsions after injecting guanidine into a fasting rabbit<sup>23</sup> similar to those noted by Titus, Dodds and Willetts<sup>1, 2, 3, 5</sup> in eclampsia. They also maintained the blood sugar levels and alleviated the symptoms in their toxic animals by injections of dextrose.

*III. Increase in Blood Uric Acid, Amino Acids, and Lactic Acid.*—Harding, Allin and Van Wyck<sup>24</sup> report an increase in blood uric acid following guanidine administration, while Blatherwick, Sahyun and Hill<sup>19</sup> found an increased amount of amino nitrogen in the blood of animals treated with synthalin. As mentioned above, Minot<sup>15</sup> has demonstrated an increase in blood lactic acid and its excretion in the urine, independent of muscular exertion.

*IV. Increase in Blood Pressure.*—Major and his coworkers have repeatedly demonstrated the pressor action of guanidine. Major<sup>21</sup> showed that the hypertension is brought about by vasoconstriction, and that this effect could be elicited, not only by parenteral administration, but also by absorption from the alimentary tract, and most readily from the ileum.

*V. Edema.*—Ellis<sup>22</sup> showed that the brain, kidney and striated muscle taken from animals in acute guanidine tetany had a higher water content than the same tissues from normal animals; and that the blood of rats similarly treated had an abnormally low water content.

*VI. Renal Damage.*—Elkourie and Larson<sup>27</sup> state that guanidine poisoning in animals results in a simple tubular necrosis of the kidney, in which the glomeruli are very little affected. Blatherwick, Sahyun and Hill<sup>28</sup> found that the administration of synthalin to rabbits caused nephritis accompanied by uremia. We, too, have certain histologic evidence of this occurrence in experimental animals.

*VII. Coagulability of the Blood.*—Major<sup>26</sup> investigated the effect of guanidine on the clotting time of the blood and found that while there seemed to be a tendency for the latter to be shortened, the variations were within normal limits, and no constant change could be shown. We plan to repeat this work.

*VIII. Convulsions.*—These are a most noteworthy accompaniment of guanidine intoxication. Frank, Stern and Nothmann<sup>27</sup> describe the characteristic differences in muscular response between cold blooded animals, the lower mammals such as the mouse and the rabbit, and higher mammals such as the cat and the dog. Using dimethyl guanidine, they were able to elicit in the cat a series of periodic convulsive seizures closely approximating those of human eclampsia. Guanidine poisoning is not always marked by convulsions but a certain number of animals (Minot's) showed merely profound depression during the intoxication. These were the animals in which Minot found the liver's glycogen stores still relatively high, but as stated before these animals received only one or two large doses of the guanidine.

In our experiments we attempted to imitate the slower progression of an eclamptic process by administering sublethal doses of guanidine over a period of time, in order to obtain a cumulative effect. Our animals generally showed a progressive lethargy, then paralysis of the hind-quarters, and presently convulsions followed by death. It was relatively uncommon not to observe convulsions in the animals treated as described.

#### TECHNICAL DETAILS OF INVESTIGATION

The development of various technical steps in the investigation which required elucidation caused our series of experiments to arrange itself into four groups. For example, even the proper dosage of guanidine and the proper frequency of its administration was uncertain and needed to be determined. Other factors are outlined below.

#### DOSAGE AND TOXICITY

Group I was that in which the toxic but sublethal and finally lethal doses of guanidine and dimethyl guanidine for rats was determined.

We desired at first to develop a toxic dosage which could be prolonged over several days so as to have a progressive, cumulative effect on the organism. It is hardly to be expected that a single, fatal dose would have time to cause much if any histologic change in the liver or kidneys, although it is on such evidence as this in some instances that conclusions have been based.

Twelve rats were treated, 6 with guanidine, 4 with dimethyl guanidine, and 2 with injections of normal salt solution as controls.

Guanidine carbonate neutralized to litmus to prevent sloughs, and dimethyl guanidine sulphate were the preparations used throughout the experiments.

In the Group I experiment the dosage of each of these varied from 0.2 gm. to 0.5 gm. per kilo of body weight, this eventually being increased if necessary to do so in order to cause death. The test was not allowed to go over fifteen days.

All animals given guanidine showed convulsions before death; 2 died after the second daily dose, one after the third, and one after 9 daily doses. The largest number of injections was ten over fifteen days, increasing the dosage from 0.2 to 0.48 gm. per kilo in two animals.

When convulsions were established four animals were killed by a sudden blow, while two died in convulsions before this was done.

Dimethyl guanidine in all instances in this and the other groups has proved more toxic than guanidine.

Two animals died after the first injection of 0.5 gm. of dimethyl guanidine per kilo of body weight.

Two received 0.2 gm. for 6 injections at daily intervals.

All 4 had convulsions.

### METHODS OF CONTROLLING EXPERIMENTS

The 2 controls were given 10 one c.c. doses of 0.9 per cent sodium chloride solution at the same intervals as the guanidine dosage.

The histologic findings in these controls were abnormal for control animals (see Table I), and we have not determined whether or not this could be due to the salt solution.

It was apparent from these, however, that neither conclusions nor assurance were to be had from a small series of controls. Obviously it would be necessary in judging the pathologic results of any treatment to have an ample series of experi-

TABLE I.

GROUP ONE: Rats Receiving Guanidine and Dimethyl Guanidine; Small Doses at Daily Intervals.

Number	Dates	Doses	Dosage per kilo body wt.	Progressive Clinical Data	Pathologic Findings
103	1-13 1-14, 72	2	Guanidine 0.5 gm.	No symptoms; Dead in rigor; still warm	Liver: Diffuse cloudy swelling; pale staining midzonal areas in which cytoplasm is foamy; periportal thrombosis; central areas lobules stain well. Kidney: Cl swelling conv tubules
105	1-13, 14, 15, 72	3	Guanidine 0.5 gm.	Mild paralysis; Spasmodic movements; Moribund Killed	Liver: Cloudy swelling periphery of lobules; hemorrhage in isolated areas with beginning necrosis. Kidney: Marked cl swelling conv tubules; desquamation lining cells; interstitial hemorrhage; debris in tubules
106	1-13, 14, 15, 16, 19, 21, 22, 23, 26, 72	9	Guanidine 0.1 to 0.5 gm	Convulsive movements; Paralysis; Carcasses Dead, Still warm	Liver: Diffuse cl swelling, intracellular hemorrhage, periportal thrombosis, isolated areas with hemorrhage with beginning necrosis. Kidney: Similar to 105
109	1-13, 15, 15, 72	3	Guanidine 0.5 gm	No symptoms 2 days; Convulsions, Killed	Liver: Moderate cloudy swelling; some interstitial hemorrhage. Kidney: Similar to 105
112	1-13, 14, 15, 16, 19, 21, 22, 23, 26, 72	10	Guanidine 0.2 to 0.48 gm	No symptoms 11 days; Torpid; Paralysis; Violent convulsions Killed	Liver: General moderate cloudy swelling in parenchyma. Kidney: Similar to 105
115	1-13, 14, 15, 16, 19, 21, 22, 23, 26, 72	10	Guanidine 0.2 to 0.48 gm	No symptoms 11 days; dyspnea; Torpid; Convulsions; Moribund, Killed	Liver: Peripheral cells normal, central cells stain poorly, mottling, indication early central change. Kidney: Similar to 105
					interstitial moderate interstitial hemorrhage interstitial chr cell infiltration some hemorrhage and suggestion of cell changes in hem areas hemorrhage in medulla diffuse cloudy swelling medullary hemorrhage to necrosis
107	1-13, 14, 15, 16, 19, 21, 22, 23, 26, 72	0	0.2 to 0.48 gm	Killed	Kidney: Similar to 105
Controls	15 days	10	NaCl 0.9%	No symptoms Killed	Liver: Intracellular hemorrhage, central; some chr. hepatitis. Kidney: Resembles 105
110	15 days	10	NaCl 0.9%	No symptoms Killed	Liver: Normal; small areas of infiltration, peripheral; some chr. hepatitis. Kidney: Resembles 105

Summary: 10 experimental animals, 2 controls. 9 of 10 showed convulsions. 2 controls apparently healthy.

Liver Changes: Cloudy swelling 9 (Peripheral 4, general 5, central 0). Hemorrhage 6 (Peripheral 2, general 4, central 0). Beginning necrosis 2; Periportal thrombosis 2; Changes in central cells 1

Kidney Changes: All specimens showed signs of irritative changes.

Controls: Showed sufficient changes from normal (livers and kidneys) to make experiment merely suggestive but inconclusive

Experiment establishes sublethal and lethal dosage guanidine for rats.

TABLE II

GROUP TWO: Rats Receiving Guanidine and Dimethyl Guanidine. Toxic Doses Daily - Lethal Effect in 4 days.

Number	Dates	Doses	Dosage per Kilo Body Wt.	Progressive Clinical Data	Pathologic Findings
205	2-25, 26, 27, 28, '32	4	Guanidine 0.35 to 0.4 gm	No symptoms until last day. Violent convulsions; Killed	Liver: Moderate cloudy swelling; small amount hemorrhage. Kidney: Moderate cloudy swelling; moderate medullary hemorrhage
211	2-25, 26, 27, 28, '32	4	Guanidine 0.32 to 0.42 gm	No symptoms until activity 3rd day. At day 4; died in rigor.	Liver: Diffuse cloudy swelling and hemorrhage, mostly central. Kidney: Cloudy swelling conv. tubules; moderate medullary hemorrhage.
214	2-25, 26, 27, 28, '32	4	Guanidine 0.3 to 0.4 gm	No symptoms until final twitching paralysis, and death.	Liver: Diffuse cloudy swelling and hemorrhage, mostly central. Kidney: Similar to 211
216	2-25, 26, 27, 28, 29, '32	5	Guanidine 0.3 to 0.6 gm	Occasional twitching, finally paralyzed; killed when moribund	Liver: Slight cloudy swelling and hemorrhage. Kidney: Moderate cloudy swelling conv. tubules and moderate medullary hemorrhage.
218	2-25, 26, 27, 28, '32	4	Guanidine 0.3 to 0.4 gm	No symptoms until final weak convulsions Killed	Liver: Isolated areas peripheral fatty degeneration, begin. necrosis and hemorrhage. Kidney: Similar to 211 but less pronounced.
226	2-25, '32	1	Guanidine 0.2 gm	Found dead, still warm and limp.	Liver: Slight cloudy swelling and little hemorrhage Kidney: Similar to 211 but less pronounced.
230	2-25, 26, 27, 28, 29, '32	5	Guanidine 0.31 to 0.70 gm	Activity; finally twitching; Killed.	Liver: Diffuse cl swelling and areas of hem. Peripheral cell damage with hemorrhage Kidney: Similar to 211.
243	2-25, 26, 27, '32	3	Guanidine 0.29 to 0.3 gm	Convulsions and twitching; Killed.	Liver: Similar to 230. Kidney: Similar to 211
244	2-25, 26, 27, 28, '32	4	Guanidine 0.3 to 0.38 gm	Convulsions and twitching; Killed	Liver: Similar to 230. Kidney: Similar to 211
245	2-25, 26, 27, 28, '32	4	Guanidine 0.28 to 0.4 gm	No symptoms until moribund Killed	Liver: Similar to 230 Kidney: Similar to 211.
209	2-25, 26, 27, 28, 29, '32	5	Dimethyl Guanidine 0.2 to 0.57 gm	No symptoms until moribund. Killed	Liver: Moderately diffuse fatty degeneration and cl swelling in periphery. Kidney: Cl swelling conv. tubules; mod hemorrhage in medulla.
217	2-25, 26, 27, '32	3	Dimethyl Guanidine 0.2 to 0.3 gm	Moribund; Killed	Liver: Mod. granular change and cl swelling in peripheral cells. Kidney: Similar to 209.
223	2-25, 26, 27, 28, 29, '32	5	Dimethyl Guanidine 0.2 to 0.46 gm	Violent convulsions, Moribund; Killed.	Liver: Moderate fatty degeneration and cl. swelling in periphery. Kidney: Similar to 209.
231	2-25, 26, 27, '32	3	Dimethyl Guanidine 0.2 to 0.3 gm	Died in rigor, autopsy while still warm.	Liver: Similar to 209. Kidney: Similar to 209.
234	2-25, 26, 27, 28, 29, '32	5	Dimethyl Guanidine 0.2 to 0.38 gm	No symptoms until last day. Apathetic. Killed	Liver: Diffuse cl swelling and areas of hemorrhage Slight peripheral cell damage. Kidney: Similar to 209.
237	2-25, 26, 27, '32	3	Dimethyl Guanidine 0.19 to 0.3 gm	3rd day moribund but still reacting vigorously Killed	Liver: Diffuse cl swelling; hemorrhage; suggestion cellular damage. Kidney: Similar to 209.
238	2-25, '32	1	Dimethyl Guanidine 0.2 gm	Found dead, diaphragmatic spasm; Still warm at autopsy	Liver: Chronic hepatitis; mod congestion separating cell columns in many areas. Kidney: Cloudy swelling.
239	2-25, 26, 27, 28, 29, '32	5	Dimethyl Guanidine 0.2 to 0.48 gm	Violent convulsions; Gasping; Moribund; Killed	Liver: Diffuse peripheral fatty degeneration and periph cl swelling Kidney: Similar to 209
240	2-25, 26, 27, '32	3	Dimethyl Guanidine 0.2 to 0.3 gm	3rd day sick, limp; Found dead; Still warm	Liver: Diffuse cl swelling; hemorrhage; suggestion cellular damage. Kidney: Similar to 209.
246	2-25, 26, 27, 28, 29, '32	5	Dimethyl Guanidine 0.2 to 0.65 gm	Violent convulsions; Coughing; Killed	Liver: Diffuse peripheral fatty infiltration. Few normal liver cells. Kidney: Similar to 209
Controls No 204 225 208 227 210 228 213 229 222 247 224	5 days 2-24 10 28, '32	5	Physiologic Salt Solution 1cc daily hypo injection	No symptoms.	Liver: All showed a certain amount of cloudy swelling; otherwise normal except 225 which showed, in addition, moderate central fatty infiltration. Kidneys: All showed slight cloudy swelling and medullary hemorrhage except 213 which showed no hemorrhage. 227 showed, in addition, interstitial cell infiltration (chronic).
Controls No. 206 232 207 233 212 235 215 236 219 241 220 242 221	5 days 2-24 10 28, '32	0	No medication for these controls; merely kept on same diet as others and killed	No symptoms.	Liver: All normal except for slight cloudy swelling. Kidneys: 232, 233, and 235 showed slight cloudy swelling; 241 moderate cloudy swelling and medullary hemorrhage; 236, 242, 206, 207, 212, 215, 219, 220, and 221 were normal. 232, 233, 235, and 241 findings much less marked than in guanidine and dimethyl guanidine series.

Summary. (a) 20 experimental animals; (b) 11 salt solution controls and (c) 13 negative controls.

(a) 11 were seen having convulsions; 2 were questionable, and 7 were not seen to have convulsions.

The size of the group made careful clinical observations difficult.

(b) and (c) All controls were apparently healthy.

Liver changes: Cloudy swelling 13 (Peripheral 6, general 5, central 2); Hemorrhage 12 (Peripheral 6, general 4, central 2);

Beginning necrosis or cell damage 8 (Peripheral 5, general 3); Fatty degen. 6 (Peripheral 5, general 1); Chr. hepatitis 1

Kidney changes: Cloudy swelling 20; Hemorrhage 19.

Controls: Liver condition described as "slight cloudy swelling" is general; all fields show uniformity; one specimen showed central fatty infiltration. Liver conditions described in experimental animals therefore represents deviation from normal.

Kidneys show practically same changes, but to a lesser degree, seen in experimental animals.

Experiment shows that guanidine compounds, in toxic doses, cause suggestive, but not specific or uniform histologic changes in liver and to a lesser degree in kidneys. From this study it was decided to abolish the 24 hour interval during which tissue regeneration could occur — see Table III.



mental animals with a similarly large series of control animals supposedly normal. In this way the general incidence of occurrence of histologic change in treated animals could be compared with that in the general run of supposedly normal animals.

Moreover, with large numbers the control series could be divided between those receiving physiologic salt solution injections, and those merely kept under the same general conditions as all, and killed about when the tested animals died. To give one group of control rats an injection of fluid comparable to the bulk of the guanidine injection determines the validity of the possible objection that this mechanical process causes infarcts and thrombosis. All animals were kept on a liberal diet, which included cracked corn in unlimited quantity.

#### LARGER DAILY DOSAGE OVER SHORTER INTERVAL

Group II experiment was conducted in practically the same way, that is, daily injections but the dosage was so planned as to cause death in four days.

This group was composed of 10 rats treated with daily doses of guanidine, 10 with dimethyl guanidine, 11 with physiologic salt solution, and 13 negative controls killed by a blow.

#### ELIMINATION OF LIVER REGENERATION POSSIBILITIES

Because the histologic examination of the tissues of the foregoing animals showed findings which were still suggestive but not conclusive a suggestion made by Dr. A. J. Bruecken was adopted. This was that the life cycle of the rat is so short as compared to that of a human being that an interval of twenty-four hours between injections allows too great an opportunity for regeneration of liver cells between doses as compared to the presumably constant formation of toxins in a preeclamptic woman.

TABLE III

GROUP THREE: Rats Receiving Guanidine: Lethal Dose Divided Into Eight (8) Hourly Intervals - Lethal Effect in One Day

Number	Date	Doses	Progressive Clinical Data	Pathologic Findings
401	3-28-32	4 Guanidine 0.125 gm	1 No symptoms 2 Lethargic; 3 Spasmodic; 3 Convulsive 4 Convulsions Killed	Liver: Scattered large vacuoles (fatty infiltration); general hemorrhagic congestion mostly around central veins. Cells stain well Kidneys: Moderate cloudy swelling convoluted tubules
402	3-29-32	8 Guanidine 0.07 gm	1 & 2 Quail 3-4 Slight spasms 5 Slight convulsions 6 7 Eating 8 Convulsions Died	Liver: Hemorrhagic congestion, mostly central, displacing in some areas liver columns around central veins Kidneys: Moderate cloudy swelling convoluted tubules
403	3-30-32	5 Guanidine 0.07 to 0.08 gm	2 Slight convulsions 3 No symptoms 4 Spasmodic 5 Paralyzed twitching died	Liver: Congestion and areas of hemorrhage with cells swollen and columns partly disintegrated with granular cytoplasm; few areas central and peripheral resembling focal necrosis Kidneys: Cloudy swelling convoluted tubules
404	3-31-32	8 Guanidine 0.063 gm	No symptoms until after 8th dose; paralysis, spasmo- philias; Killed	Liver: Moderate congestion; generalized cloudy swelling cells with moderate breakage of columns Kidneys: Moderate cloudy swelling convoluted tubules
405	3-31-32	8 Guanidine 0.062 gm	No symptoms until after 8th dose; paralysis, spasmo- philias; Killed	Liver: Occasional oval vacuole (fatty infiltration) Moderate central congestion; section stains uniformly Kidneys: Moderate cloudy swelling convoluted tubules
406	3-31-32	8 Guanidine 0.062 gm	No symptoms until after 8th dose; paralysis, spasmo- philias; Killed	Liver: Moderate congestion especially around central vein. Scattered single cells with fatty degeneration and infiltration Kidneys: Slight cloudy swelling convoluted tubules
Controls 407 410 408 411 409 412	3-31-32	0 No medication	Normal animals Killed by stunning blow, and bleeding	Livers: No cellular change; poor histologic sections (technical). Kidneys: Slight cloudy swelling convoluted tubules; less than changes noted in experimental animals.

Summary: 6 experimental animals, 6 controls 3 of 6 had convulsions; all were 500 g.

Liver Changes: Cloudy swelling, general 1; Hemorrhage 6 1 General 2, central 4; Fatty infiltration or degeneration 3 1 General 2, central 1; Necrosis 1.  
Kidneys: Cloudy swelling conv. tubules 6.

Controls: Livers negative; Kidneys show moderate cloudy swelling.

Experiment developed more suggestive evidence of liver damage in fatty changes within and between cells.

Consequently in Group III 12 rats were utilized. Six were given hourly injections of guanidine, each dose being one-eighth of the lethal dose. Six untreated controls were examined.

## UTILIZATION OF ANIMALS WITH PLACENTATION SIMILAR TO HUMAN BEINGS

In Group IV guinea pigs were utilized because their placentation resembles that of the human being. We have been impressed with the fact that the work of Dieckmann<sup>23, 28</sup> is the only one which seems to have approached by experimental formation the lesions thought of by many to be typical of eclampsia; namely the focal necrosis in the periphery of the liver lobules.



Fig. 1.—Liver from Rat No. 103; guanidine injections (Table I). Shows mottling due to differences in staining qualities of cells in various areas; beginning thrombosis in portal vein branch.

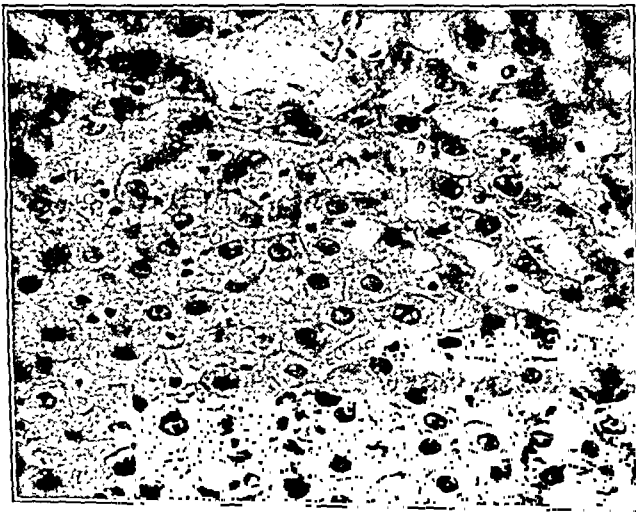


Fig. 2.—Same as Fig. 1; high power. Shows congestion, swelling and "foamy" cytoplasm, also breaking-up of liver cell columns in certain areas.

Dieckmann's suggestion that syncytial tissue and chorionic villi may be a source of tissue fibrinogen exciting this lesion is a reasonable one, and we plan in our next work to determine whether or not the combination of dimethyl guanidine injections into animals that are pregnant, will go any further toward completing the chain of evidence being investigated. The question of the mechanical effect of these injections arises although even complete obstruction of the portal vein does not cause necrosis of liver tissue. Closure of branches of the portal vein as in thrombosis may

result in hemorrhagic infarcts, which latter while being "death" of tissue do not present the same picture as focal necrosis.

We found in Group IV that guinea pigs were more resistant to the dimethyl guanidine injections than rats had been.

Four guinea pigs were used for the experiment and 2 were killed as controls. These animals required 12 injections daily over four days, and of course the element of regeneration during the night intervals must be considered.

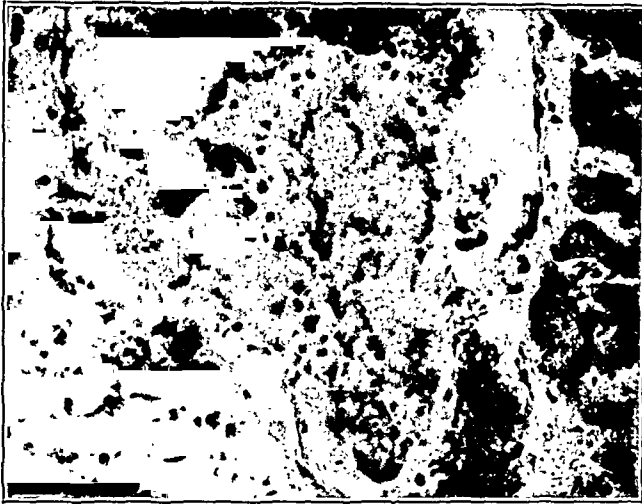


Fig. 3.—Liver from Rat No. 108 (Table I); high power, showing thrombosis branch of portal vein.

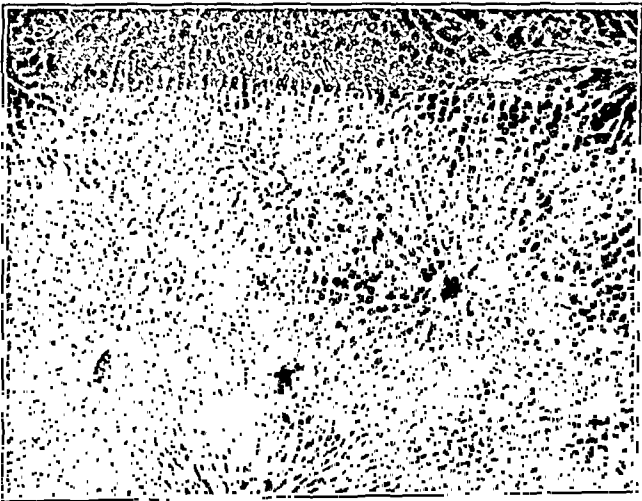


Fig. 4.—Liver from Rat No. 113 (Table I); shows congestion around central vein, beginning breaking-up of liver cell columns.

The Group IV experiment resolved itself essentially into an investigation to determine the toxic and lethal dosage of dimethyl guanidine for guinea pigs when given at hourly intervals, thus being somewhat similar to that of Group III for rats.

This links up so closely with the projected work just discussed that it seems advisable to say for the present, merely that the organs of these animals showed degenerative changes similar to those outlined in the three tables. This can be discussed more in detail in connection with the investigation now under way, which is mentioned now merely as a preliminary report.



Fig. 5.—Same as Fig. 4; high power, cloudy swelling and congestion noticeable.



Fig. 6.—Liver from Rat No. 209 (Table II). Marked fatty degeneration in periphery of lobules.

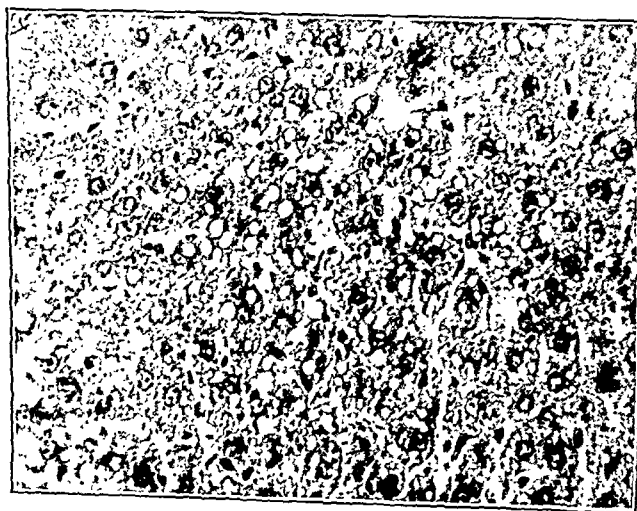


Fig. 7.—Same as Fig. 6; high power. Beginning necrosis also noticeable.

## DISCUSSION OF HISTOPATHOLOGIC RESULTS

The foregoing details have been summarized in order to eliminate them from and thus condense the tables.

The results are shown in detail in Tables I to III and in Figs. 1 to 14.



Fig. 8.—Liver from Rat No. 246 (Table II). Peripheral fatty degeneration ("infiltration") and beginning necrosis.

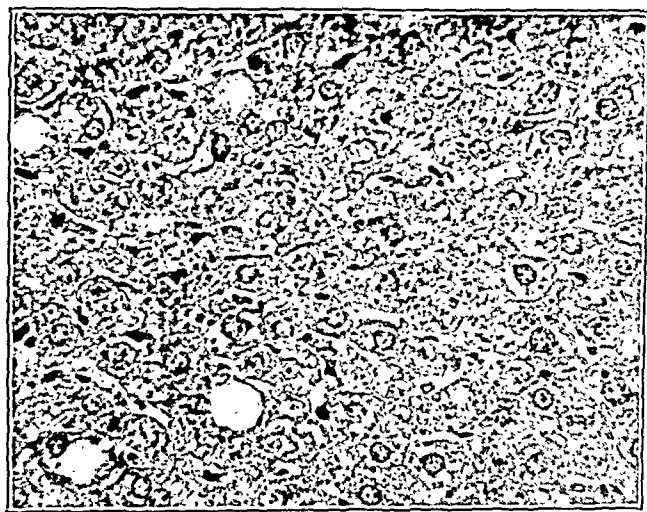


Fig. 9.—Same as Fig. 8; high power. Shows swelling, granular and fatty changes in cytoplasm with loss of cell outline.

The recent important clinicopathologic study of eclampsia by Acosta-Sison<sup>30</sup> who performed complete autopsies on 38 patients has raised anew the question as to the specificity of any liver lesions in eclampsia. It is true that many authorities, notably Williams,<sup>31</sup> have regarded peripheral necrosis in the lobule as the characteristic liver lesion in eclampsia. In summarizing these 38 autopsies, Acosta-Sison says "focal areas of hemorrhagic necrosis and fatty degeneration predominantly in the periphery of the liver lobule were observed only in a few cases (4 cases), the liver lesions were rather scattered indistinctly (this may be a misprint for

indiscriminately) in the lobule with special susceptibility for the central areas." Acosta-Sison finds that hemorrhagic, fatty, and degenerative changes may affect the eclamptic liver alone or in combination.

Fatty degeneration, according to Beattie and Dickson<sup>22</sup> may be regarded as a retrogressive change associated with the appearance of fatty granules or globules in

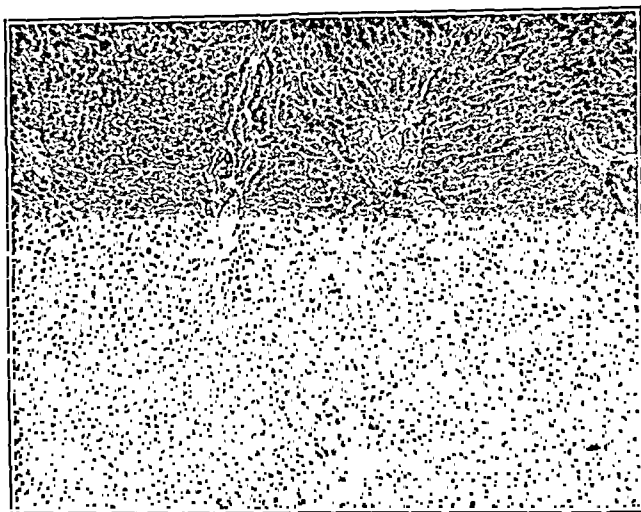


Fig. 10.—Liver from Rat No. 403 (Table III). Focal necrosis, both central and peripheral.

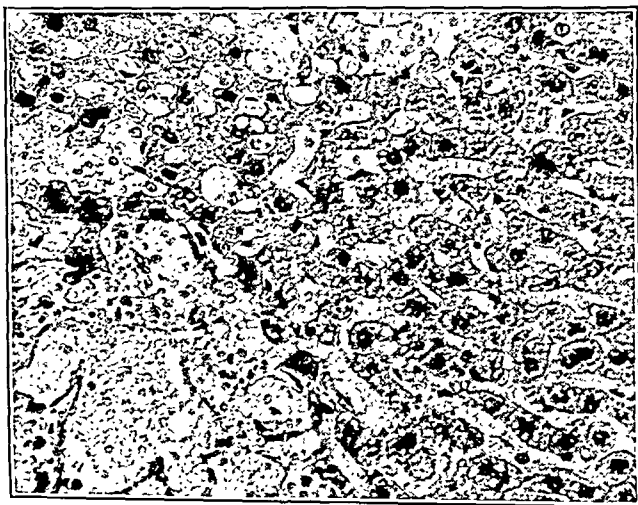


Fig. 11.—Same as Fig. 10; high power. Shows edges of areas of focal necrosis, hemorrhage, granular cytoplasm.

the cytoplasm of the cell, this being one of the common methods of decay in the animal cell. It frequently occurs as a sequel to, or in combination with cloudy swelling. Fatty infiltration and other degenerative conditions are frequently found associated with fatty degeneration. They quote authorities who state that the term "fatty degeneration" conveys a wrong impression and should be termed "degenerative fatty infiltration" as being an encroachment of fat from the outside deposited within cells whose vitality is lowered so that they cannot use it up.

The foregoing is a prelude to the statement of the impression which we have gained from these series of animals which were given toxic doses of guanidine or dimethyl guanidine. Suggestive changes in their livers have developed, such as cloudy swelling, interstitial hemorrhage, beginning periportal thrombosis, and fatty infiltration and degeneration both

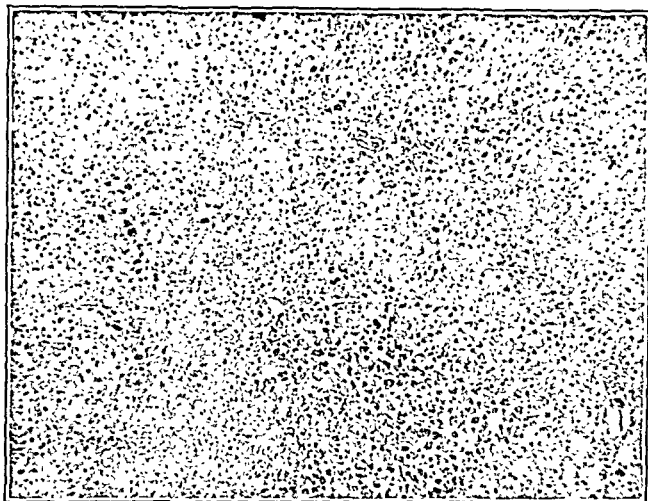


Fig. 12.—Human eclamptic liver (low power). Shows cloudy swelling, hemorrhage, and focal necroses both central and peripheral.



Fig. 13.—Kidney from Rat No. 238 (Table II). Shows cloudy swelling of convoluted tubules; desquamation lining cells; debris in tubules.

peripheral and central, as well as differences in the staining qualities of the cells in various areas of the liver lobules. All of these are illustrated in Figs. 1 to 14, and the ones showing peripheral and central focal necrosis are especially interesting in view of the opinions held by some on this subject.

We are not satisfied that these histologic alterations represent anything more than early degenerative changes, similar perhaps to those

found in about 29 per cent of Acosta-Sison's eclamptics, and we do not feel that true focal necroses were produced in any more than one of these animals despite the suggestive appearance of some of the photomicrographs. At the same time we are still unconvinced that this latter is an invariable and characteristic feature of eclampsia.

The histologic changes noted in the kidneys were thought to be strikingly typical of toxic irritation until those of the control animals were examined. In practically all of those to which the guanidine substances were given, it was noted that cloudy swelling of the convoluted tubules, with desquamation of the lining cells, debris in the tubules, and interstitial hemorrhage occurred. That this did not represent as profound a change as at first thought, was demonstrated by the finding that this was also the case to a lesser degree in many of the control

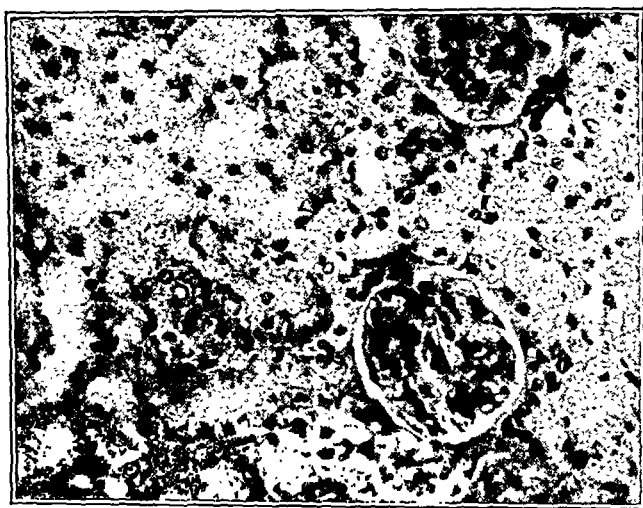


Fig. 14.—Kidney from Rat No. 403; high power. Marked cloudy swelling and desquamation.

animals. It was usually possible to distinguish between a control and an experimental animal's renal tissue and to say that the control more nearly represented normal, but cloudy swelling of some degree occasionally accompanied by medullary hemorrhage were almost constant occurrences in the kidneys of apparently healthy control animals.

It is suggestive and of interest that there is a metabolic toxin which can so accurately reproduce in animals the major clinical symptoms of eclampsia, and likewise develop some of the histopathologic changes seen in this disease. This experiment was conducted on nonpregnant animals and the positive results which have been obtained in the form of degenerative histologic changes in the liver and kidneys seem to be sufficiently convincing to warrant carrying the experiment further.

The next step as stated above is to duplicate the details of the Group IV experiment in animals advanced in pregnancy and having the same type of placentation as human beings.



## SUMMARY

1. Several investigators have now demonstrated various biochemical or metabolic disturbances in eclampsia, such as fluctuations in blood sugar during the attack, and a trend toward hypoglycemic levels. Increase in blood uric acid and lactic acid, increase in blood pressure, edema, albuminuria, and convulsions are commonplace symptoms.

2. Reports have been made of an increase in guanidine-like substances in the blood during preeclampsia and eclampsia.

3. By experimental administration of guanidine compounds to animals all of the foregoing clinical symptoms of eclampsia may be reproduced, including the fluctuations in blood sugar and typical convulsive seizures.

Moreover, the clinical use of certain guanidine compounds in reducing blood sugar levels in diabetics, as a substitute for insulin, has now been abandoned because of its toxic effects and its tendency to cause sudden and profound hypoglycemia.

4. Authorities have differed as to whether the increased apparent guanidinemia in instances of acute liver injury, either clinical or experimental, precedes and causes the liver tissue degeneration, or follows it having resulted from this tissue destruction.

5. The experimental injection of a single dose or two of a guanidine compound sufficient to kill an animal quickly should not be expected by an investigator to produce much if any histologic changes in the tissues of liver and kidneys, because of the abruptness of its action.

6. This experimental investigation was undertaken to determine whether or not a more or less protracted series of guanidine and dimethyl guanidine injections would, by their cumulative action, cause histopathologic changes in the liver and kidneys.

7. Degenerative changes of varying types but chiefly suggestive of early stages of hepatic degeneration have been produced in a large, controlled series of animals. These changes include cloudy swelling, interstitial hemorrhage, beginning periportal thrombosis, and fatty degeneration and infiltration both peripheral and central, as well as focal necroses similarly distributed. The kidneys showed cloudy swelling of the convoluted tubules, desquamation of lining cells, and hemorrhage.

8. These hepatic changes were less distinctive in the animals to which guanidine injections were given by single daily doses than in those receiving the injections at hourly intervals to the point of death in one day. In the former, liver cell regeneration probably takes place during the resting period. It was, for example, by the latter method that the 6 animals (Group III) were treated, of which one showed the focal necroses in the liver referred to in the preceding paragraph.

9. It is of interest that experimental administration of a metabolic toxin which can be elaborated within the body can reproduce in animals

the major clinical symptoms and at least the early stages of the histopathologic changes seen in eclampsia.

10. The exact source of an accumulation of guanidine-like substances within the body is still uncertain, and their relation to eclampsia is entirely problematic.

11. Tables detailing the pathologic findings in this series of experiments are given, and numerous photomicrographs of liver and kidneys are shown.

The authors desire to express their thanks for the technical assistance given by Miss Mary Beam.

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1015 HIGHLAND BUILDING.

# RECONSTRUCTION OF THE OVIDUCTS: AN IMPROVED TECHNIC WITH REPORT OF CASES\*

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WITH the increased interest in the study and the revision in the treatment of sterility, plastic surgery upon the oviducts has rapidly advanced and has found a definite place in gynecologic surgery. New and improved procedures have been frequently reported, and the end-results have shown marked advancement. However, the majority of the authors of these papers judge their results by the number of pregnancies following such procedures.

The proper evaluation of any plastic operation upon the oviducts, in our opinion, does not necessarily rest upon the percentage of cases of pregnancy following, but upon the percentage of patent oviducts after operation.

Bilaterally occluded oviducts classify sterility as absolute, and, as Meaker aptly states, "the initiation of the reproductive process is, at any rate for the time being, flatly impossible." With the oviducts remaining patent after operation, the problem becomes one of relative sterility, and the initiation of the reproductive process not definitely impossible.

This study was not primarily instituted as a problem in sterility, but with the idea of developing a new technic, or improving upon the old, in operations upon occluded oviducts to maintain patency.

Although the number of cases herein reported is small, the technic has been so developed that the procedure is now being presented for your consideration and trial. Thus a larger number of cases may be reported in the future, and a more extensive evaluation placed upon the operation and its end-results. The cases studied were selected from those ward patients who, after proper tests, were found to have bilateral tubal occlusions, while also requiring other corrective pelvic operations for retroverted uteri, prolapsed adnexal masses and ovarian cysts. Thus this study was not made as a purely experimental one at the inconvenience of the patient. No special consideration was given to age or marital status.

## CLASSIFICATION OF TUBAL OCCLUSIONS

For the purpose of this study, tubal occlusions have been classified as follows:

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1. Outer third, which includes those occurring in the ampullary portion, and those resulting in occlusion at the fimbriated extremity (Fig. 4).

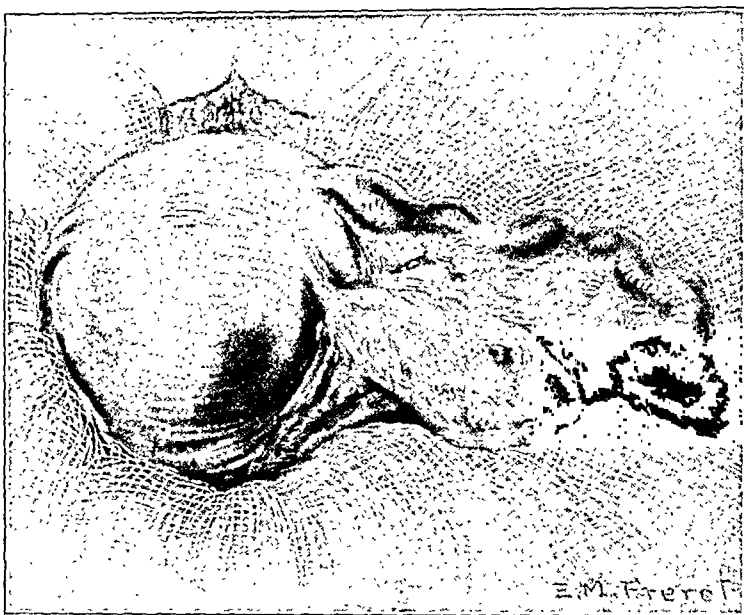


Fig. 1.—Salpingitis isthmica nodosa. Inner two-thirds occlusion.

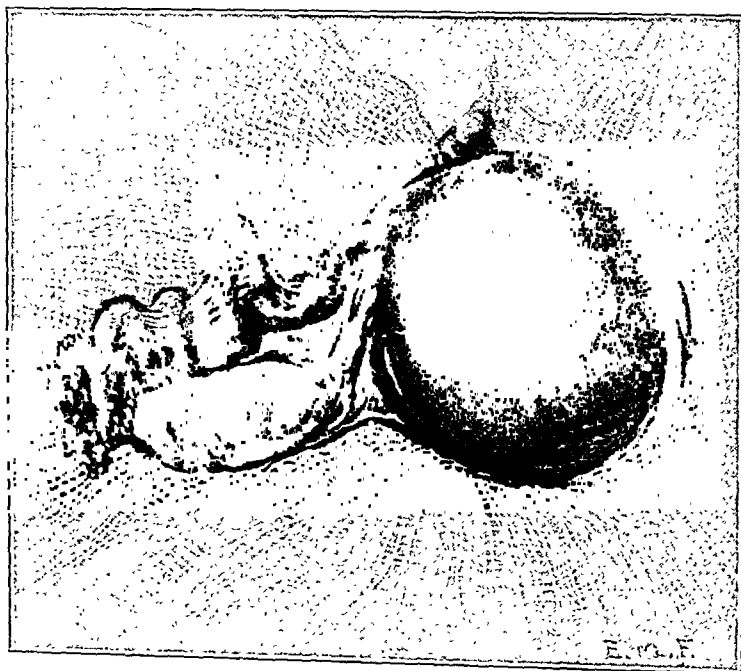


Fig. 2.—Occlusions due to kinks caused by adhesions.

2. Occlusions occurring in the inner two-thirds of the tube anywhere in the isthmie or interstitial portions (Fig. 1).

Extratubal conditions leading to occlusions, such as kinks, adhesions, or pressure by tumors, were not considered (Figs. 2 and 3).

This classification was made due to the fact that two distinct operative procedures are indicated depending upon the site of occlusion.

#### SELECTION OF PATIENTS

It is obvious that this operation is intended for the correction of absolute sterility, and therefore the patients selected for this procedure should be in the childbearing age, free from any developmental stigmata, and the husband proved fertile. Cases exhibiting acute or subacute pelvic pathology or tuberculous salpingitis are not suited to this procedure.

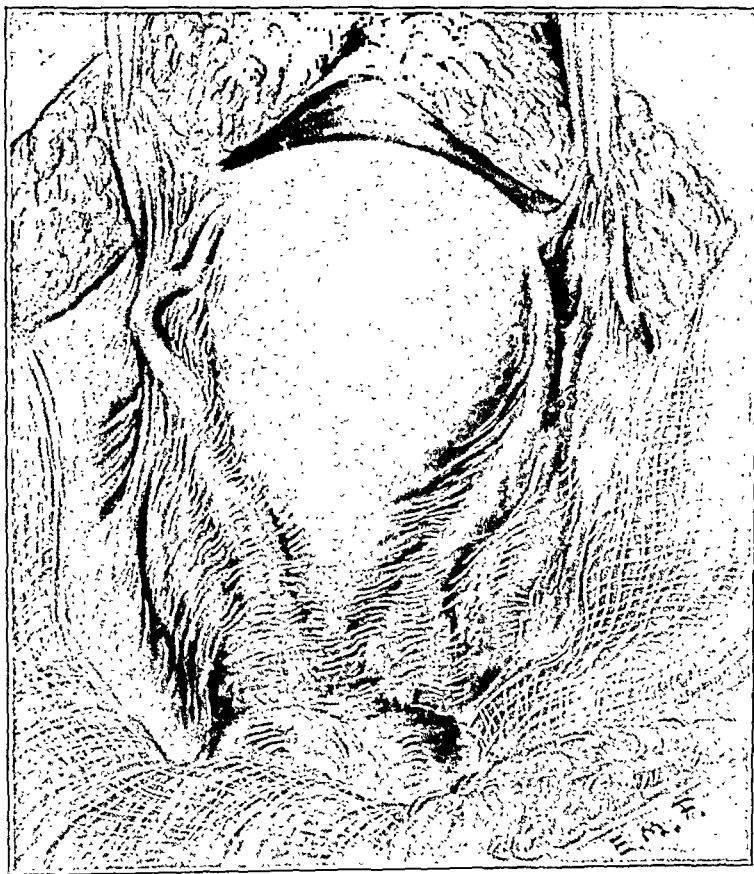


Fig. 3.—Occlusions caused by adhesions with prolapsed adnexa.

Patients with chronic adnexal disease are not acceptable until they have been under observation for at least three menstrual periods and the leucocytic count, temperature and sedimentation time show no variation from normal after bimanual examination. Patients operated upon for pathologic conditions other than sterility are at times well suited for this procedure.

#### PREOPERATIVE PREPARATION

Proper attention to detail in the preoperative preparation makes for the success of the end-results.

All local foci of infection in the cervix, Skene's ducts, and Bartholin's glands must be eliminated, and a Rubin insufflation test performed.

In order to assist in the recovery of the diseased tissues by a process of resolution or regeneration, the patient receives a series of treatments consisting of the application of heat per vaginam. At Bellevue we have adopted the Elliott method for this purpose. Holden and Gurnee have reported the results of this treatment in all types of pelvic infection, and it was found at the time of operation, in those cases requiring subsequent celiotomy, that inflammatory adhesions had either been absorbed or become filamentary, the previously diseased tissues appeared to be firm instead of friable, and the edema so often seen at time of operation was absent.

The number of treatments given in this series of cases varied from a minimum of 12 to a maximum of 28. The treatment was given daily for

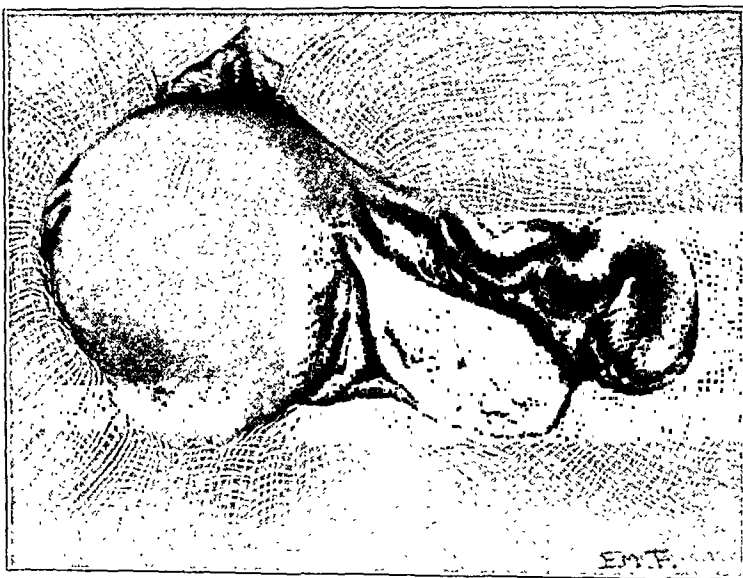


Fig. 4.—Occlusions occurring in outer third of tube, so-called clubbed tube.

a period of forty-five minutes at  $128^{\circ}$  F., at least three to four weeks before operation.

The criteria in determining the number of treatments to be given any individual are: diminution in the size of adnexal masses, or the inability to palpate adnexa previously palpable.

As these treatments at times may, by the absorption of the proliferative inflammatory process, lead to reestablishment of the patency of the tubes, the insufflation test should be repeated. The most suitable time for the operation is during the intermenstrual period.

A hysterosalpingogram was obtained pre- and postoperatively in a few of the cases for corroboration of the findings of the insufflation test.

#### OPERATIVE TECHNIC

Following the classification previously mentioned, oviducts having occlusions in the outer third are reconstructed by performing what we

have termed a "circumcision" operation as suggested by Bonney, everting the tube by bringing back the mucosa to the serosa for a distance of 1.5 cm. to 2.5 cm., thereby eliminating raw surfaces at the newly constructed ostium and avoiding adhesions and occlusions which are so prone to follow plastic operations.

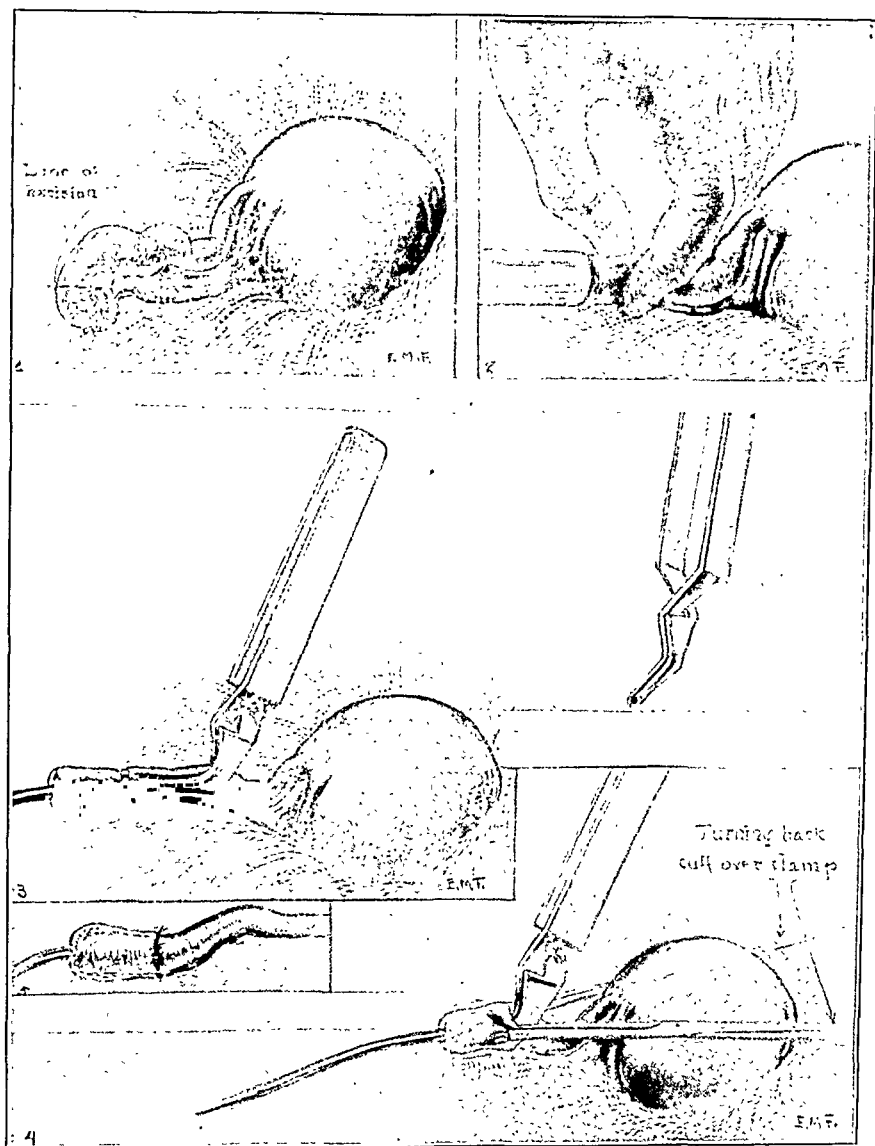


Fig. 5.—"Circumcision" operation for reconstruction of occlusions occurring in outer third of tube. 1, Line of amputation proximal to site of occlusion. 2, Testing patency of remaining portion of tube. 3, Insertion of silk bougie and application of Bonney clamp  $1\frac{1}{2}$  to  $2\frac{1}{2}$  cm. from amputated end. Circular incision down through muscularis. 4, Turning back cuff over clamp everting tube. Mucosal cuff being brought back to serosa. 5, Cuff anchored to serosa. Reconstruction complete.

Oviducts showing occlusions anywhere in the inner two-thirds are not suitable for the circumcision procedure, but are suitable for the implantation operation to be described shortly.

This implantation procedure attempts to maintain the normal anatomic and physiologic relationship of the tube to the uterus.

1. "*Circumcision*" *Technic*.—The tubes are handled without instruments in order to avoid trauma. The fimbriae, if occluded, are freed by blunt dissection, or if the tube be clubbed an amputation is performed proximal to the site of occlusion (Fig. 5, 1). Bleeding is controlled by the use of mosquito clamps and No. 00 plain liga-

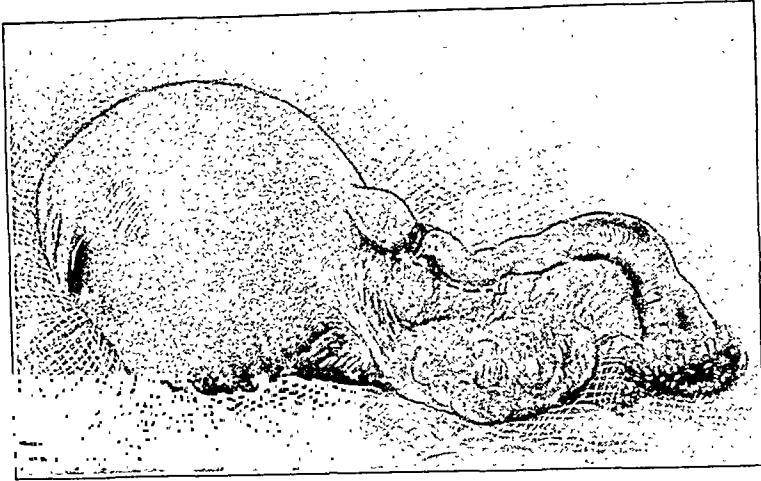


Fig. 6.—Amputation of tube proximal to site of occlusion. Site determined by use of intrapelvic insufflation syringe.

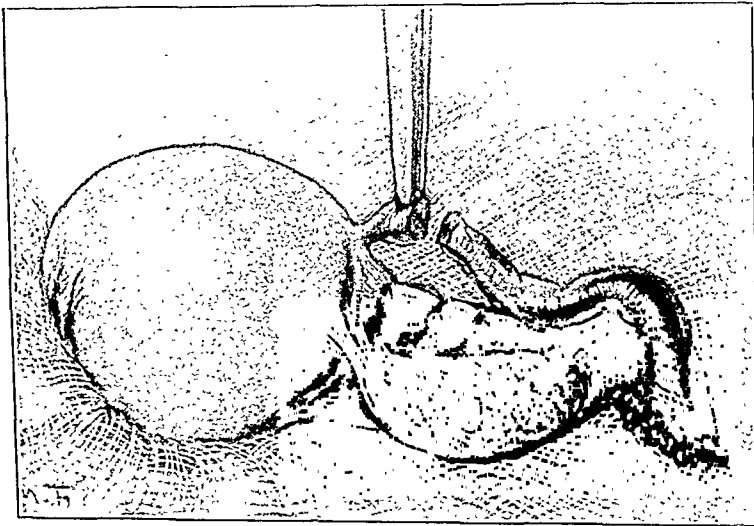


Fig. 7.—Freeing uterine portion of occluded tube from its attachment to the broad ligament. Also freeing patent portion of tube from broad ligament for a distance of one-half cm.

tures. The remaining portion of the tube is then tested for patency by air insufflation with the use of the glass syringe as suggested by Curtis (Fig. 5, 2). If patent, the air entering the uterine cavity produces a gurgling sound, and if the fundus be held, a vibratory impulse is transmitted to the fingers. If the tube be occluded at any other site it becomes dilated by the insufflated air proximal to the occlusion, and the gurgling and vibration are not present. If the remaining portion of the tube is found patent, a straight silk catheter, size No. 9 to 12 French, is inserted into the



outer third of the tube. A Bonney clamp is then placed over the tube and its inserted catheter, 1.5 cm. to 2.5 cm. from the amputated end. A circular incision is made at the distal end of the clamp down through the muscularis (Fig. 5, 3). Two fine Allis clamps are then applied to the amputated end of the tube, gently pulling it backward while the Bonney clamp is slowly pushed forward; thus the mucosa is everted and brought back to the serosa (Fig. 5, 4). This tubal cuff is held in place

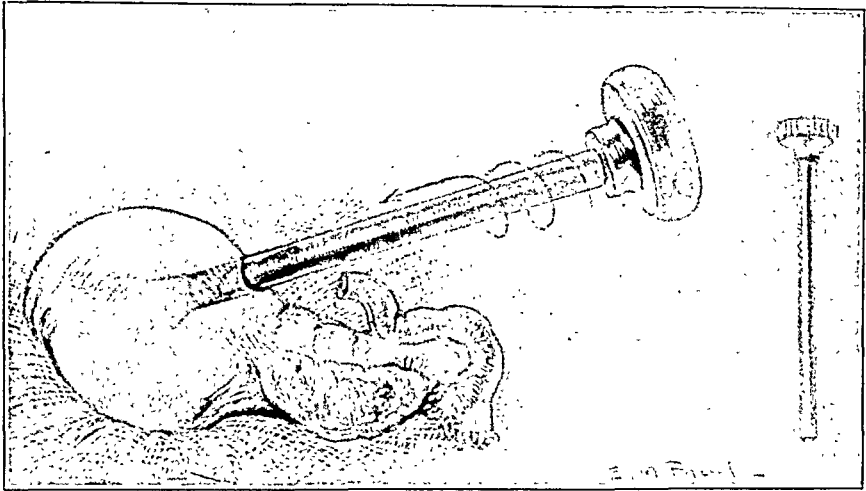


Fig. 8.—Reaming instrument applied over occluded stump of tube. With a circular movement of the instrument stump of the tube and its intramural portion is reamed out.

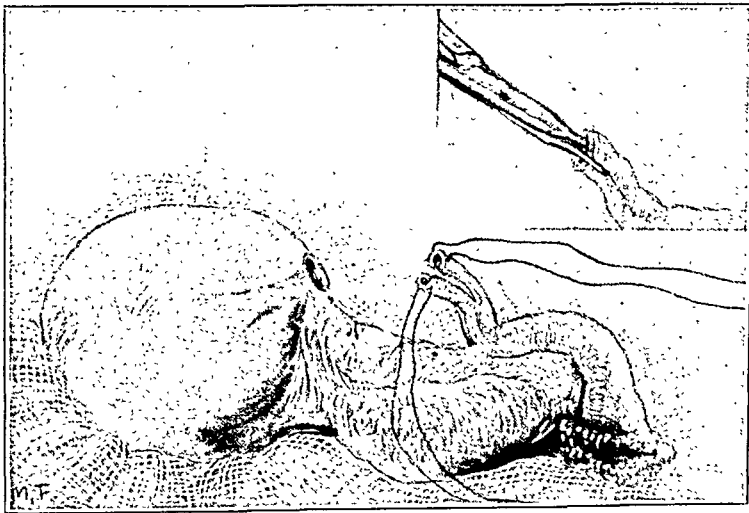


Fig. 9.—New opening into uterus following removal of occluded tube and its intramural portion. Patent portion of tube bisected longitudinally by cuticle scissors. Long No. 00 chromic sutures applied to superior and inferior ends of bisected tube.

by three interrupted No. 00 plain sutures placed so that they are concealed beneath the end of the cuff. The Bonney clamp is then gently released and removed with the catheter (Fig. 5, 5). The patency of the reconstructed tube is again tested by air insufflation with the use of the glass syringe (Fig. 5, 2). Following this the tube and ovary are suspended from the side wall of the pelvis by taking a small bite through the pelvic peritoneum and the hilum of the ovary with linen suture, according to the Poole technic (Figs. 12 and 13). It is well to bring the height of this

suspension almost level with the round ligament. This procedure prevents the adnexa from prolapsing and becoming adherent in the culdesac and also relieves the congestion due to previous stasis by reestablishing a more normal circulation. A one point suspension of the uterus is performed in order to keep the uterus out of the culdesac.

2. *Implantation Technic.*—The site of the occlusion is again noted by air insufflation and the tube is severed proximal to the occluded area until a free passage of the insufflated air is evident (Fig. 6). The uterine portion of the occluded tube is then freed as far as the cornu from its attachment to the broad ligament, cutting as close as possible to the tube, in order to avoid impairment of the ovarian circulation. Bleeding vessels of the broad ligament are clamped and tied with No. 00 plain gut (Fig. 7). The uterus is firmly held while a specially constructed reaming instrument is passed over the occluded stump of the tube. The tube and its intramural portion is reamed out by a circular movement of the instrument entering the uterine cavity and maintaining as nearly as possible the normal position and course of the

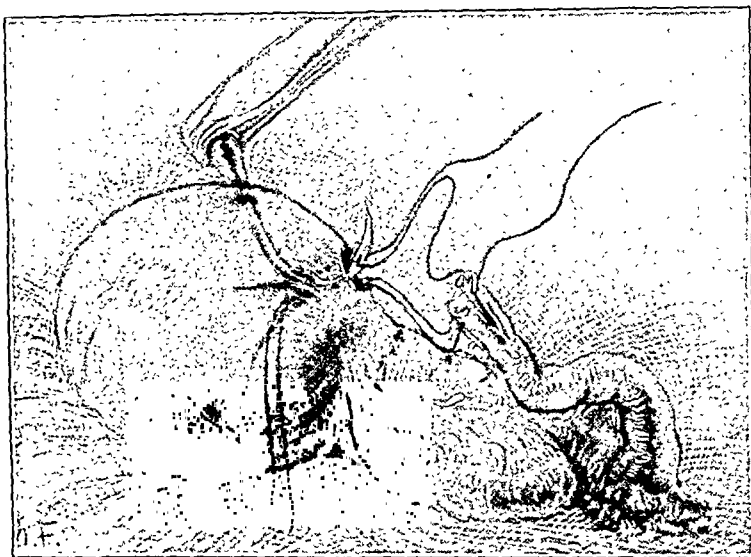


Fig. 10.—Insertion of Reverdin needle 1 cm. beyond center of fundus posteriorly passing out through the newly created uterine opening, in order to bring out the suture previously applied to the end of the superior portion of the bisected tube. The same procedure followed by insertion of the Reverdin needle through anterior surface of the fundus.

tube (Fig. 8). A core remains consisting of the old occluded stump of the tube and the chronically infected cornual tissue which is readily removed when the reamer is withdrawn. The new opening into the uterus will have a diameter of approximately 0.5 cm. This instrument does not produce any free bleeding as might be expected in this area, due to the fact that the circular motion crushes rather than cuts the blood vessels. The slight amount of oozing first noted quickly subsides. The patent portion of the tube is also freed from its broad ligament attachment for a distance of about 0.5 cm., bleeding controlled, and then bisected longitudinally by cuticle scissors, guided by a probe inserted within its lumen (Fig. 9).

Through the superior and inferior ends of the bisected tube a long No. 00 chromic suture is passed and the ends of the suture clamped for further use (Fig. 9). A Reverdin needle is inserted about 1 cm. beyond the center of the fundus, posteriorly, passed out through the newly created uterine opening and the ends of the suture previously applied to the superior bisected portion of the tube reinserted into the eye of the needle, the needle withdrawn, and the sutures brought out on the posterior

surface of the uterus without tension. The same procedure as above is repeated by passing the Reverdin needle through the anterior surface of the fundus and bringing out the suture on the inferior portion of the bisected tube (Fig. 10). The serosal covering of the bisected portion is traumatized and by gently pulling the anterior and posterior fundal sutures, the tube is gradually drawn into the newly created opening and its ends into the uterine cavity. The sutures are then anchored on the fundus and two or three fine supporting sutures are passed through the serosa of both tube and uterus (Fig. 11). The patency of the newly implanted tube is again tested by the use of the insufflation syringe. The reimplanted tube and ovary are suspended by the Poole technic and the uterus by a one point suspension as previously described.

Occlusion may occur at different points in each tube, or there may be an occlusion in one tube at both the inner and outer ends, thus requiring both procedures for proper reconstruction.

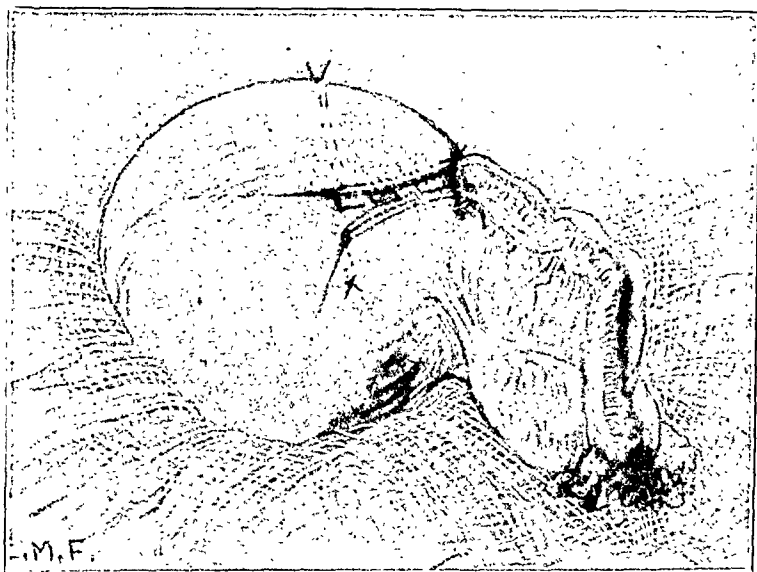


Fig. 11.—By gentle traction on the anterior and posterior fundal sutures on the previously applied anterior and posterior fundal sutures, the tube is gradually drawn into the newly created uterine opening and its end into the uterine cavity. The sutures are then anchored on the fundus. Two or three fine supporting sutures are passed through the serosa of both tube and uterus.

#### POSTOPERATIVE TREATMENT

Forty-eight to ninety-six hours after operation the patient is subjected to a Rubin insufflation test to determine and maintain patency of the reconstructed tubes. This procedure should not be attempted if any cervical or vaginal plastic operations have been performed or if the patient shows a marked postoperative reaction.

Before the patient is discharged from the hospital this test is repeated to insure the patency of the tubes. If, however, the tubes are patent on discharge from the hospital, patient returns for follow-up at the end of three to four weeks and the patency is again determined by the Rubin test.

Although there has been a minimum of trauma in these operative procedures, sufficient tissue reaction may occur to produce temporary occlusion. It is very surprising that following the heat treatment by the Elliott method, the occluded oviducts again become patent. Therefore the operator should not become discouraged if, upon the discharge of the patient, the tubes appear to be occluded.

A striking example may be cited. One of our cases having extensive pelvic pathology due to postabortal sepsis followed by a marked gonorrheal infection, failed to show patency of the reconstructed tube for a period of eight weeks. Following fourteen Elliott treatments postoperatively, the tubes were shown to be patent both by the Rubin test and a hysterosalpingogram.

For the last six months we have employed the Elliott treatments in all of our cases after discharge, whether the tubes were patent or occluded. This helps to re-absorb any marked tissue reaction following operation.

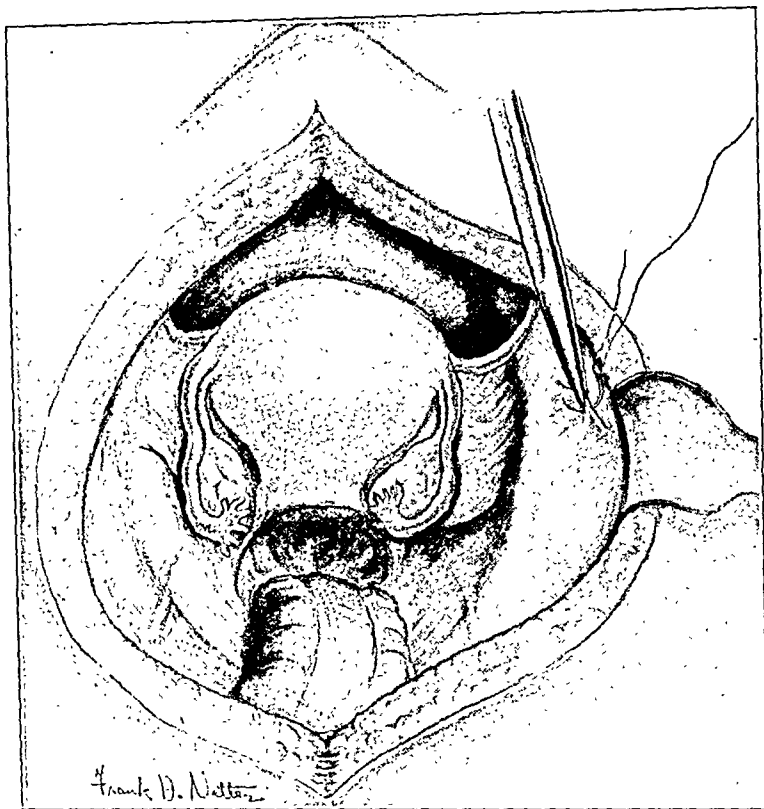


Fig. 12.—Poole's suspension. Suspending tube and ovary from side wall of pelvis. Small bite of peritoneum being taken from side wall of pelvis with linen suture.

#### POSTOPERATIVE END-RESULTS

Ten patients having bilateral occluded oviducts were studied and operated upon. The diagnosis of occlusion was made in the majority of the cases preoperatively by the transuterine air insufflation method of Rubin, in a few by the hysterosalpingogram, and confirmed in all by the intrapelvic insufflation test as originally suggested by Curtis, at the time of celiotomy.

As previously stated, no special consideration was given to age or marital status in this study. In addition to the tubal occlusions, other pelvic pathology requiring correction in this series of cases was as follows: adherent retroflexion, 5 cases; marked antelexion, 1 case; dermoid cyst, 1 case; "tary" cyst of the ovary, 2 cases; torsion of a large hydro-

salpinx, 1 case; marked laceration with pseudoadenoma of the cervix, 1 case.

Of the ten patients, seven had a reconstruction operation, performed for occlusion of the outer third of the oviduct. These were divided as follows: reconstruction of both tubes, 2 cases; reconstruction of the right tube, 4 cases; the left tube being so diseased as to require removal or having been removed at a previous operation; reconstruction of the

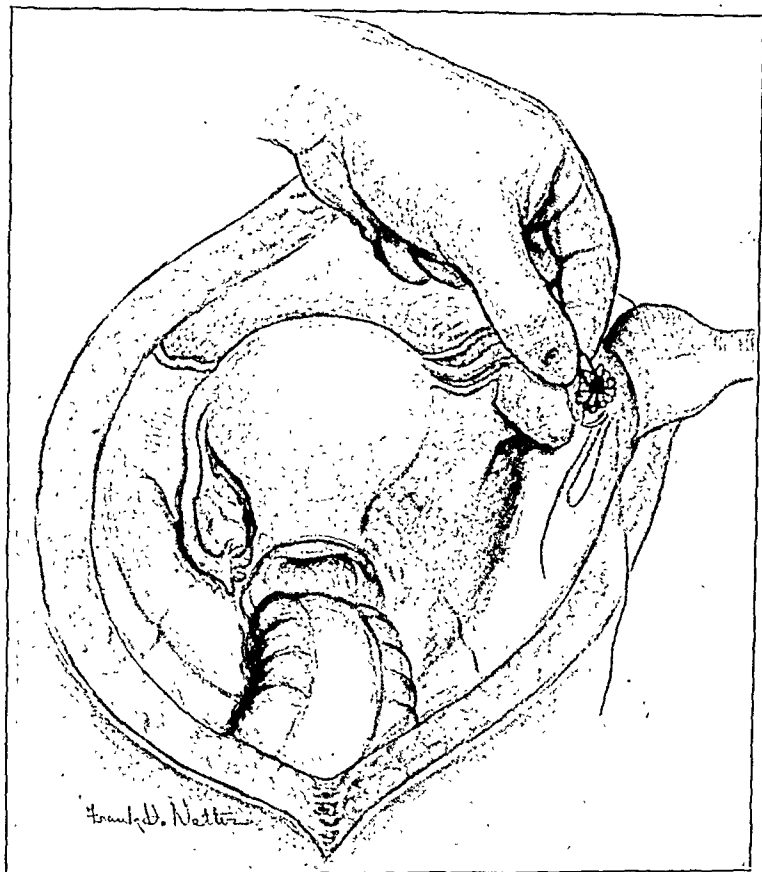


Fig. 13.—Poole's suspension. Small bite taken through hilum of ovary in order to suspend tube and ovary. This suspension prevents tube and ovary from prolapsing into culdesac.

left tube, 1 case, right tube in this case being cord-like and completely occluded.

Five of the above 7 patients having had the so-called "circumcision" operation have patent oviducts as proved by the transuterine insufflation test and by a hysterosalpingogram. It is fair to mention that one of the two cases classified as having nonpatency after operation did not have any tests performed, as these were contraindicated before discharge from the hospital. This patient had an amputation of a markedly infected cervix. She has never returned for examination and cannot be located by our social service.

The remaining three patients of this series of ten had an implantation operation performed for occlusion occurring in the inner two-thirds of the oviduct. These tubes showed a salpingitis isthmica nodosa. The left tube was implanted in one case, the right tube being cord-like in its entire length. The right tube was implanted in the second case, the left tube showing a large hydrosalpinx requiring removal, and in the third case both tubes were implanted.

Two of the implantation cases have patency as proved by the usual tests before mentioned.

In this series of 10 patients having operations performed for occluded oviducts, seven, or 70 per cent, show patency. To correct the statistics by omitting the one patient who failed to return for tests and examination, the percentage of patients showing tubal patency after operation is 77.7 per cent.

As previously stated this study was not primarily instituted as a problem in sterility. It is, however, of interest to mention that one of the patients having an implanted tube became pregnant three months after operation, and had a normal delivery of a full-term, viable child. And another having had a reconstruction of the outer third of both tubes is now three months pregnant, fourteen months after operation.

#### SUMMARY

1. Tubal occlusions for the purpose of this study were classified as those occurring in the outer third of the tube, and those occurring in the inner two-thirds of the tube.
2. Two distinct operative procedures were instituted for reconstruction.
3. The so-called circumcision operation was performed for occlusions occurring in the outer third of the tube.
4. The implantation operation was performed for occlusions occurring anywhere in the inner two-thirds of the tube.
5. Seven of the 10 patients operated upon, or 70 per cent, have patent tubes after operation. The corrected percentage of patency after operation is 77.7 per cent.

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59 EAST FIFTY-FOURTH STREET.

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## CHEMICAL CHANGES IN THE PARTURIENT'S BLOOD\*

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CHEMICAL research in gynecology and obstetrics deals with a very unusual situation. During menstruation, pregnancy, labor, and puerperium, the blood chemistry of the woman is normally and regularly changed, in comparison with the normal average findings. These phases are most important and frequently lead to pathologic changes. We must, therefore, determine the normal condition during these certain phases of the sexual life of the woman, before undertaking the investigation and explanation of pathologic deviations.

Our knowledge today concerning these normal changes is still quite incomplete. Much work has been done on the normal physiologic chemistry of pregnancy, but even here there are many disagreements. Our knowledge of the normal chemical changes, which are brought about by labor in the body of the mother, is much more incomplete. Labor is an event of such decisive effect that we must expect considerable change in the chemistry of the body. Careful investigation in this direction seems to be absolutely necessary.

Most investigators have restricted themselves to one or, at the most, two series of observations during labor and have called their findings "the general labor value." Very soon after the beginning of our work we found that labor could not be comprehended as a uniform event from the chemical viewpoint. During the different stages of labor varying changes take place in the body chemistry of the mother.

Labor is usually divided in the physiologic sense into the following stages: (1) Dilatation, (2) expulsion, and (3) placental stage. We have found that this division does not apply to the chemical changes. The changes which take place during the first stage of labor and the longest part of the second stage (second A-stage) are less marked than those that take place during the last minutes of the expulsion stage. This part, which we will call the second B-stage, is the actual time of real birth, from the appearance of the head in the introitus to the complete expulsion of the child.

Every stage of labor must be investigated separately in order to grasp the changes which occur during it. A more thorough and separate investigation of the second B-stage was undertaken. The first stage and the second A-stage were studied together. Of course, a separate investi-

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\*Read, by invitation, before the American Gynecological Society, May 30 to June 1, 1932, at Québec, Canada.

gation would be more desirable. Thus, our experiments were divided into four parts:

- I First and second A-stage of labor.
- II Second B-stage of labor.
- III Third stage of labor.
- IV Investigation of the puerperium during the fifth or sixth days postpartum.

Furthermore, normal nonpregnant women were investigated as controls.

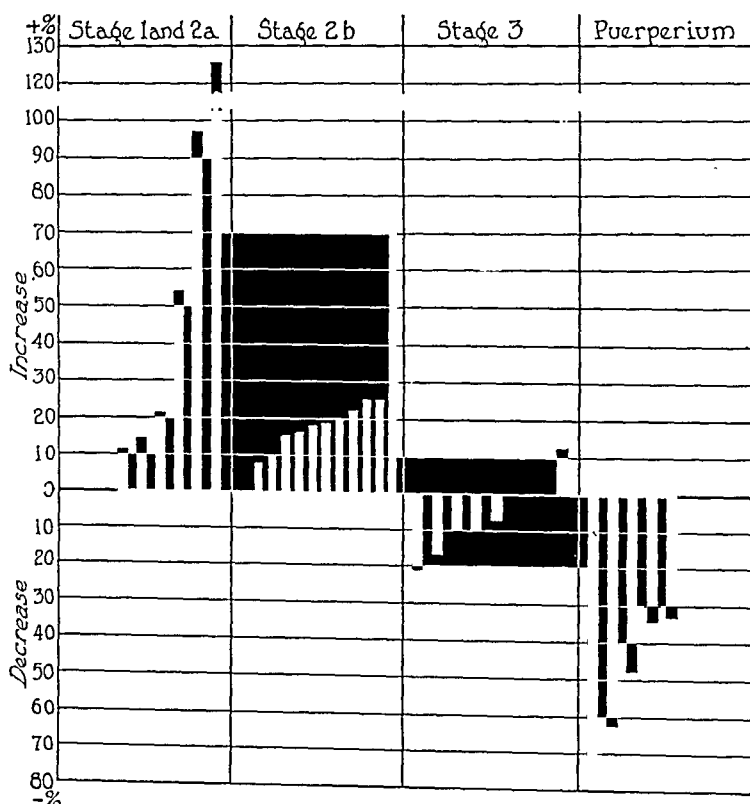


Fig. 1.—Changes in the acetone content during labor expressed in percentage.

The investigations included only absolutely normal parturients who received no medicine or anesthesia of any kind. The blood was taken from the cubital vein without compression. The most reliable technic was used and the blood examined for the amount of ketone bodies (acetone, diacetic acid, and  $\beta$ -oxybutyric acid), nonprotein nitrogen, blood sugar, hydrogen ion concentration, water content, dry residue, total nitrogen, refraction, etc. In some cases the urine was also examined.

To determine the ketone bodies, a procedure which was quite similar to the Engfeldt method was used. In nine normal cases investigated for control, we found acetone, 1 to 1.57 mg. per cent, and  $\beta$ -oxybutyric acid, 5.75 to 11.75 mg. per cent. These amounts corresponded to the findings of other authors.



Figs. 1 and 2 show the changes which occur in the *acetone and  $\beta$ -oxybutyric acid* content of the blood during the different stages of labor. They represent graphically the four different parts of the investigation mentioned above. The effect of every phase was investigated separately by taking one specimen of blood at the beginning and another at the end of the phase. In the charts the absolute height of the finding is not reported, but the relative changes which occurred during the different phases are expressed as percentage of the first value (the value found at the beginning of the phase). Each column represents one case. The

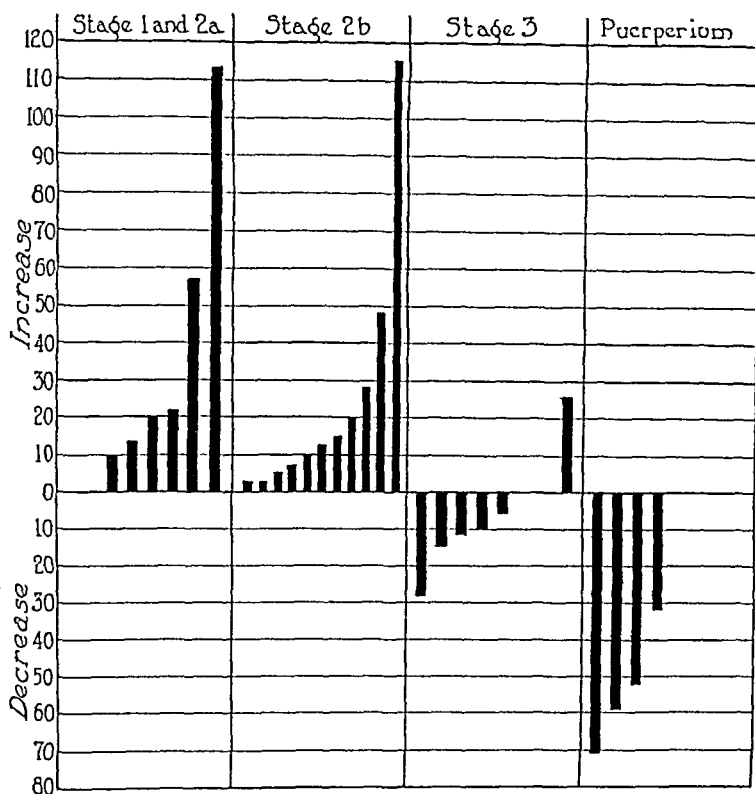


Fig. 2.—Changes in the  $\beta$ -oxybutyric acid content during labor expressed in percentage.

downward trend designates a decrease and the upward an increase. The effect of labor upon the acetone and  $\beta$ -oxybutyric acid contents is very significant, as is shown by the illustrations.

In Part I of the investigation, the first blood specimen was taken at the beginning of labor and the second immediately before the birth of the child. During the stage of dilatation and the first part of the expulsion stage, an increase of the acetone and  $\beta$ -oxybutyric acid content of the blood occurred in all cases. In some the first value was doubled.

Part II concerns itself with the delivery of the child (second B-stage). The first specimen of blood was taken just before the head passed through the introitus, and the second immediately after the birth but before the umbilical cord was tied. The average interval between the two veni-

punctures was only nine minutes, the longest time being sixteen minutes and the shortest four minutes. The figures show that as marked increases occurred in most of the cases during this short time as during the period of several hours in Part I of the investigations. The comparison of time indicates that something entirely different must have taken place during the few minutes in Part II than in the number of hours in Part I. The influences effecting the blood chemistry during the second B-stage of labor are, therefore, not merely a continuation of those operating in the first and second A-stage.

Part III comprises the placental stage. The first specimen of blood was taken immediately after the birth of the child and the second after the expulsion of the placenta. Here the tendency towards a decrease in the amount of ketone bodies in the blood predominated.

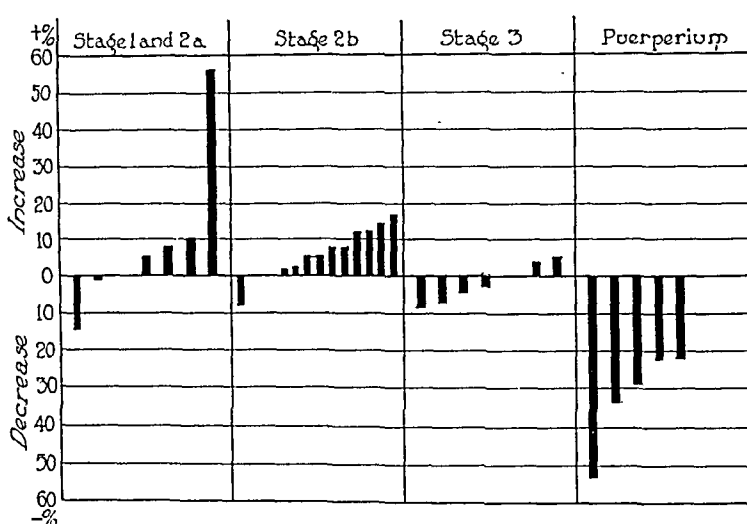


Fig. 3.—Changes in the blood-sugar content during labor expressed in percentage.

During Part IV, comprising the puerperium, a marked lowering of the values of acetone and  $\beta$ -oxybutyric acid was seen. The absolute values found in the puerperium corresponded with the general normal average. Therefore, the marked decrease is a sign that the values during labor are considerably higher than the normal values in nonpregnant patients.

The blood sugar was determined by the method of Hagedorn-Jensen. In twelve normal nonpregnant cases, from 74 to 97 mg. per cent of blood sugar were found, which corresponded to the normal average.

Fig. 3 shows the changes in the amount of blood sugar. They are not as uniform as those of the other mentioned substances. From this, perhaps, one may conclude that the changes in the blood sugar during labor are due to more varied influences than those of the ketone bodies. During the dilatation stage and the first period of expulsion, we found both an increase and a decrease, the increase predominating. The case with

a marked decrease showed also other deviations. The delivery of the child was, in most instances, associated with an increase in the blood sugar. Varying and weak influences seemed to effect the blood sugar during the placental stage, giving slight increases or decreases. The remarkable decrease during the puerperium, shown in the fourth part of Fig. 3, proves that during labor the values must have been relatively high.

The nonprotein nitrogen was determined with the Kjeldahl method. In nine normal nonpregnant cases we found from 19.6 to 40.0 mg. per cent. Fig. 4 shows the changes during labor. During Part I, a marked increase took place in most of the cases. During Part II (second B-stage), the rise predominated. A decrease occurred in most of the cases

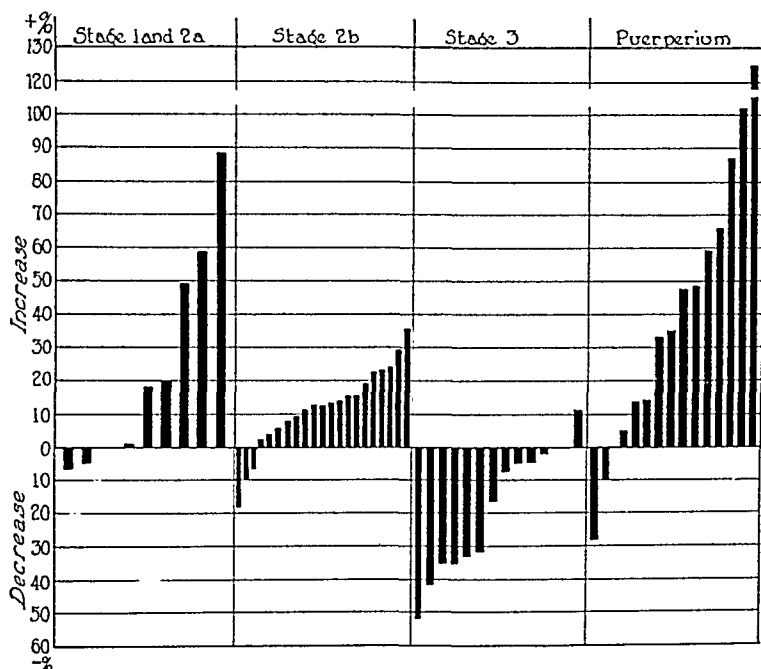


Fig. 4.—Changes in the nonprotein nitrogen content during labor expressed in percentage.

during the placental stage. A very marked increase could be seen again during the puerperium. The two exceptions may be partly explained by the fact that these cases had very high values during labor.

Fig. 5 illustrates the changes in the hydrogen ion concentration. It is drawn upon another principle than the preceding figures, the changes being noted in absolute values and not expressed in percentages. About 400 determinations of  $P_H$  were included in this chart, which made it impossible to sum them up singly. Therefore, the average values are given, but variations from the average were extremely rare.

The horizontal lines correspond to the values of the  $P_H$  at 38° C. The shaded zone between  $P_H = 7.37$  and  $P_H = 7.40$ , shows the sphere of the values found in 23 normal nonpregnant women. All  $P_H$  determinations were made with the electrometric method.

The curve is divided vertically into three sections: Pregnancy, labor, and puerperium. Pregnancy was included in the  $P_H$  examinations because we have done special work on this subject and have obtained results which are different from those of former investigators.

According to the older literature the augmentation of acids in the blood during pregnancy was an absolute certainty. Later, following the articles of Hasselbalch and Gammeltoft, the doctrine of the "compensated acidosis of pregnancy" was universally accepted. This theory was included in every textbook, but the differentiation between actual and compensated acidosis was not always very clear. Insufficient attention has been given to the investigations of Michaelis, who examined the blood

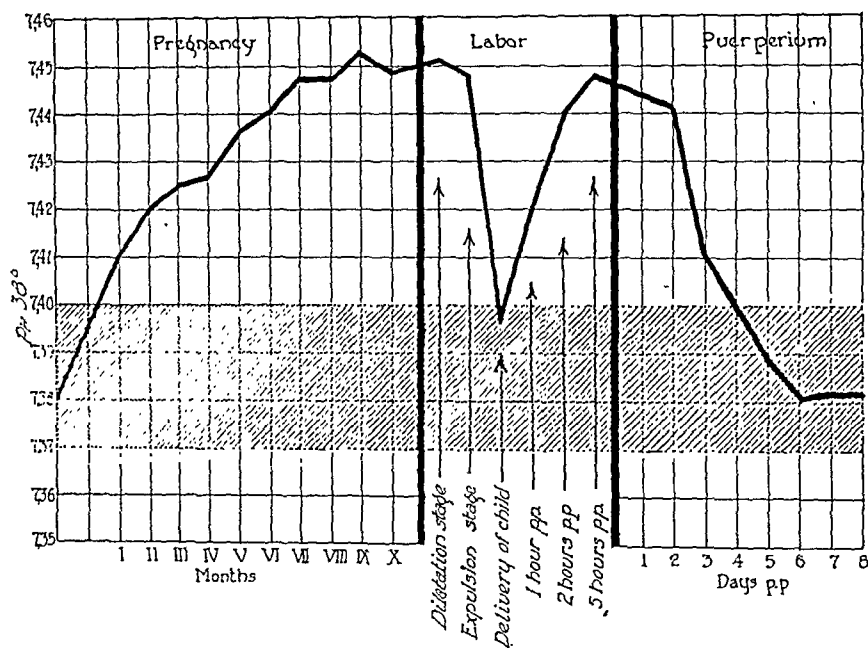


Fig. 5.—The hydrogen ion concentration during pregnancy, labor, and puerperium.

$P_H$  in some cases of pregnancy with the electrometric method, and found a slight shifting to the alkaline side. Later Bock, using the same method, noted a slight shifting to the acid side. To clarify this question, Eissner and the author made electrometric  $P_H$  determinations in a large number of cases. We proved that there is at least no actual acidosis.

In the German literature, the doctrine of acidosis of pregnancy, at least of a compensated one, still holds. Recently Anselmino acknowledged a slight actual alkalosis of pregnancy, but believes that there is, in spite of this, a compensated acidosis. He states further that he could prove an augmentation of unknown acids in the blood during pregnancy by electrometric titration.

In the American literature, the doctrine of acidosis of pregnancy seems to have lost ground for a longer period of time. For instance, Kydd states that there is no "acidosis of pregnancy." He found that the un-

known acids were not increased during pregnancy, as did also Oard and Peters. Marrack and Boone have proved a shifting of the  $P_H$  to the alkaline side by colorimetric investigations.

Other English and American authors have also made determinations of the  $P_H$  during pregnancy, but, in spite of the results, Oard and Peters wrote as follows in 1929: " $P_H$  determinations on sera in pregnancy by methods of sufficient accuracy are as yet not available in the literature." Our investigations, of which the results are reproduced in the illustrations under discussion, should be sufficient to supply this lack.

As shown in Fig. 5, the value of the  $P_H$  is higher even in the first month of pregnancy than in the normal nonpregnant cases. This increase continues with little variation until the ninth month, which means progressive shifting to the alkaline side up to this time. The slight decrease during the tenth month is probably due to the beginning of the first weak uterine contractions.

During the stage of dilatation we find approximately the same value as during the last month of pregnancy. During the expulsion stage only a very slight shifting to the less alkaline side becomes apparent; so up to the very last moment of labor there is no considerable change in the actual  $P_H$  of the blood, in spite of all labor pains.

At the very moment of birth a sharp decrease takes place. Within a few minutes a change towards the acid side occurs, which is seven times greater than that which took place during the hours or even days of labor. This shifting persists for a remarkably long time. It takes five hours before the  $P_H$  returns to the average value which existed during the first stages of labor.

TABLE I. COMPARATIVE VALUES OF THE  $P_H$  DURING THE DILATATION STAGE, IMMEDIATELY BEFORE AND AFTER BIRTH OF THE CHILD

NO.	NAME	AGE	TIME OF FIRST VENIPUNCTURE BEFORE BIRTH	TIME OF SECOND VENIPUNCTURE BEFORE BIRTH	TIME OF THIRD VENIPUNCTURE AFTER BIRTH	1. VAL	2. VAL	3. VAL
1	R	24	14 Hr. 9 Min.	2 Min.	4 Min.	7.44	7.44	7.39
2	Sch	24	5 Hr. 22 Min.	1 Min.	3 Min.	7.43	7.42	7.38
3	F	34	9 Hr. 5 Min.	2 Min.	2 Min.	7.45	7.44	7.39
4	R	23	1 Hr. 9 Min.	1 Min.	4 Min.	7.44	7.43	7.39
5	H	20	6 Hr. 11 Min.	5 Min.	3 Min.	7.44	7.44	7.39
6	K	23	9 Hr. 38 Min.	4 Min.	2 Min.	7.46	7.45	7.40
7	M	27	4 Hr.	5 Min.	4 Min.	7.45	7.45	7.40
8	W	22	6 Hr. 32 Min.	2 Min.	9 Min.	7.45	7.44	7.39
9	L	26	4 Hr. 23 Min.	2 Min.	2 Min.	7.46	7.45	7.40
10	H	20	7 Hr. 54 Min.	2 Min.	4 Min.	7.45	7.45	7.39

During the puerperium we observed a slow decrease to the values found in nonpregnant women. The most remarkable finding was that the  $P_H$  during the first days postpartum was the same as during pregnancy, and the actual reaction did not return to the normal value until several days later.

Fig. 5 shows average  $P_H$  values. Table I indicates that every single case followed the same rule. The first blood specimen in these cases was taken at the beginning of labor, the second immediately before, and the third immediately after the birth of the child. The findings show that there is very little or no shifting in the  $P_H$  value during the time of dilatation and the second A-stage, but that a sudden marked change to acid takes place during the time of the actual birth of the child.

The other blood examinations, total nitrogen, reflection index, erythrocyte count, etc., were done in order to investigate the changes in blood concentration during labor. The result was as follows: During Part I of the experiments, the dilatation stage and the main part of the expulsion stage, an increase of the concentration was found. During the period of the actual delivery of the child a marked decrease in the concentration of the serum took place. An even more marked decrease occurred during the placental stage.

We will now consider briefly the theories for the changes found in the different periods of labor.

In Part I of the investigations, that is, during the first and second A-stage of labor, we have observed the following: Marked increase of acetone and  $\beta$ -oxybutyric acid, increase of blood sugar in most cases, increase of nonprotein nitrogen in nearly all cases, no marked change in the hydrogen ion concentration (a most interesting fact), and slight concentration of the blood.

An explanation of these changes presents some difficulties, because they occur over a long period of time, in which many accidental influences may take place. The most interesting observation is a negative finding, namely, the lack of change of the  $P_H$ . The intensive muscular work should produce a large amount of acid. Indeed, several investigators found a marked increase in the amount of lactic acid. An augmentation of the acidic ketone bodies has been proved by us. The organism, however, is able to neutralize and eliminate entirely all these acids during the whole course of labor up to the very last stage. We found a remarkable acidification of the urine during labor as a result of this elimination.

The increase in the amount of ketone bodies may be best explained by the insufficient nutrition of the parturient, in connection with the strong muscular efforts.

The increase of the blood sugar is probably due to nervous influences, especially an irritation of the sympathetic system. Endocrine disturbances, with eventual increase of adrenalin in the blood, probably assist in this phenomenon. Furthermore, the increase of lactic acid and ketone

bodies raises the amount of blood sugar. There is no reason to believe that the elevation of the blood sugar during labor is a sign of hepatic change, which is the opinion of some authors.

The increase of nonprotein nitrogen, after considering all possible explanations, is probably due to a slight retardation of the renal function during labor.

The concentration of the blood must be traced back to the muscular effort and the loss of water by perspiration, respiration, etc.

On the whole, we have observed that the changes which occur in the maternal body during the hours or even days of the first and second A-stage, are not extremely marked. It is all the more surprising that during the brief second B-stage, much more marked changes take place in the substances investigated. The comparison of time alone proves that it is impossible to consider these last minutes of labor as a simple continuation of the long first and second A-stage. It is impossible to explain the changes that occur by an accentuation of labor pains at the very end of labor. Even if there were some extremely strong pains they could never bring about more changes than the entire preceding period of labor. We, therefore, believe that during the real delivery of the child new and important influences are at work. The following changes were noted during this stage of labor: Marked increase of the ketone bodies, increase of blood sugar, elevation of the nonprotein nitrogen, enormous shifting of the blood  $P_H$  to the less alkaline side, and slight dilution of the blood.

These findings and the short time in which the changes occurred, suggest the opinion that there is a sudden influx of acid substances in the blood during the real delivery of the child from some repository. We believe that the sudden reduction in size of the uterus is the main cause. Through reduction the blood and lymph fluid, which is contained in the uterine wall and the intervillous space, is pressed out and brought into the general circulation. In consequence of the labor pains and the metabolism of the fetus, this fluid contains many by-products of metabolism, most of them acid in character. This theory may be proved by the conduct of the different substances.<sup>1</sup>

During the *placental stage* the following changes were observed: Decrease in the ketone bodies, no uniform behavior of the blood sugar, decrease of the nonprotein nitrogen, no change of the  $P_H$  or a slight shifting to the alkaline side, and marked dilution of the blood.

The explanation is simple. The main factor in this change is the loss of blood and its consequent dilution by tissue fluid. Another part is the after-effect or retrogression of the labor changes. The fact that there are several antagonistic influences present explains the lack of uniform changes in this stage of labor.

During the puerperium there was a marked decrease of the amount of

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<sup>1</sup>*Siedentopf, H.: Die Physiologische Chemie der Geburt. Ambrosius Barth, Leipzig, 1932.*

ketone bodies and blood sugar, an increase of the nonprotein nitrogen, and a gradual lowering of the hydrogen ion concentration.

These changes indicate the gradual return of the organism to the normal nonpregnant state. The most interesting part of this phenomenon is that it takes several days and, as other investigations show, even months, until this return to normal is completed. So the changes during pregnancy, such as the alkalemia, cannot be due alone to direct influences of the fetus and the placenta.

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### DELIVERY THROUGH A SPURIOUS BIRTH CANAL\*

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A PRIMIPARA at term was successfully delivered of a six pound infant after a labor of twenty-four hours. The membranes ruptured spontaneously two hours after the onset of pains, and it was a vertex presentation which began as a posterior and rotated naturally to the left anterior position. The feature of this case relates entirely to the cervix and the unusual mode of dilatation which occurred. She was examined three times rectally and once vaginally immediately before removal to the delivery room where labor was terminated by medium episiotomy and low forceps. Immediate examination of the cervix showed that the external os was intact and that the child had delivered through an artificially created passage in the posterior wall of the cervix at or near its middle third. The descending head apparently had impinged upon this area of the cervical canal so vigorously and had compressed it to such thinness as to force it to give way. The aperture thus created was closed with interrupted catgut sutures but unfortunately union failed to occur. Inspection of the cervix several months postpartum revealed nothing unusual in its appearance, but when pulled forward so as to expose its entire posterior aspect, the accessory birth canal could be demonstrated as a cervico-vaginal fistula, and a sound could be passed through the real external os, into the true cervical canal and out again into the posterior vaginal fornix. Here then is a woman who was not examined vaginally until the very end of a twenty-four-hour labor, and in whom, possibly because of this, the obstetrician failed to recognize an abnormal situation which conceivably might have been averted with the more accurate information obtainable by vaginal palpation.

37 EAST SIXTY-FOURTH STREET.

\*Read at a meeting of the Obstetric Section of the New York Academy of Medicine, November 24, 1931.



## CONSIDERATION OF A NEW VIEWPOINT ON THE ETIOLOGY OF RENAL TUBERCULOSIS IN WOMEN\*

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**A**T THE beginning of the present century the medical profession was fairly well informed on the desirability of early diagnosis and radical surgery in renal tuberculosis. And yet in spite of the great advances in urology since that time, our views concerning the etiology and therapeutics of renal tuberculosis have changed but little.

Some of you may remember that about thirty years ago there was prevalent an idea that renal tuberculosis in women occurred more frequently in the right than in the left kidney. It was thought that the greater mobility of the right kidney interfered with its drainage and thus favored a more frequent incidence of tuberculosis on this side.

In September, 1903, I read a paper before the Medical and Chirurgical Faculty of Maryland on "Tuberculosis of the Urinary System in Women,"<sup>1</sup> reporting on 35 cases which had occurred in the service of Howard A. Kelly and his associates in Baltimore. In this list of 35 patients 17 were operated upon for tuberculosis of the right kidney and 18 for tuberculosis of the left, 5 of the series probably having bilateral renal tuberculosis. This experience seemed to explode the theory that the disease occurs more frequently on the right side because of impaired drainage.

In spite of the more recent work on ureteral stricture, showing the influence of interference with drainage on practically all of our so-called surgical diseases of the kidney, it was not until about seven years ago that my attention was again called to the possibility that defective drainage might have an important etiologic bearing on renal tuberculosis. My first report on a series of stricture cases was entitled, "Stricture of the Ureter, Excluding Tuberculosis and Calculus; Report of Fifty Cases."<sup>2</sup> I soon found that our former ideas concerning the sequence of events in the formation of ureteral stone and its surrounding infiltration with inflammatory tissue were probably erroneous, and two years later I published arguments to show that in most instances the ureteral stricture is primary and the encased stone secondary.<sup>3</sup> Since then I have published a number of articles containing facts which seem to demonstrate that one cannot discuss the etiology of calculus of either ureter or kidney without a full consideration of ureteral stricture.

More recently facts have been accumulating to demonstrate that the title of my first report on ureteral stricture is further subject to criticism because of its implication that the type of stricture under discussion was not associated with tuberculosis of the upper tract. Up to the present time we have all taken it for granted that the frequent obstructive conditions found in the ureter in association with renal tuberculosis are specific in nature and are directly derived from the diseased kidney.

In about 1925, or nine years after my first publication on ureteral stricture, I became gradually impressed by the fact that I was seeing a considerable number of patients who had undergone a nephrectomy for tuberculosis, and who had returned months or years later because of

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\*Read at the Fifty-Seventh Annual Meeting of the American Gynecological Society, May 30 to June 1, 1932, at Quebec, Canada.

For lack of space, this article cannot be printed in the JOURNAL as presented, but appears in complete form in the author's reprints, as well as in the current volume of the Society's Transactions.

symptoms referable to the remaining kidney. On going over history records I was surprised to find that I had been consulted by 15 patients belonging in this category. Since 1925 two more of our former patients who have had nephrectomies have returned because of stricture symptoms on the other side. In 2 of these 17 cases the symptoms were apparently due to a wide open ureteral orifice and free reflux of urine from the bladder to the kidney, causing renal pain as the bladder and upper tract became distended. Both of these patients had been under my care for a monolateral renal tuberculosis, and at that time had been found to have extensive inflammatory involvement about the base of the bladder, and I attributed the subsequent loss of the valvular control of the ureter to the action of scar tissue after healing of the bladder had taken place. Whether these two patients had originally had ureteral stricture could not be determined because of the widely dilated ureteral lumen at the time of final consultation.

In the other 15 patients we found, on their return, no evidence of infection in the remaining kidney, and their symptoms were apparently due to ureteral stricture as determined by the bulb test, pyeloureterograms, and the satisfactory results of treatment by simple dilatation.

These experiences gradually forced the question: were these strictures present on the supposedly normal side at the time of the removal of the other kidney for tuberculosis? We know that simple ureteral stricture is practically always bilateral, and we know that serious damage from stricture may result to both kidneys without a complaint of any kind. We also know that the patient with bilateral stricture may localize the symptoms on one side, while investigation shows the symptomless side to be the one more damaged. Hence it must be insisted that absence of symptoms on the supposedly normal side at the time of a nephrectomy for tuberculosis does not preclude the presence of ureteral stricture on this side. An occasional patient with unilateral tuberculous kidney complains of pain only on the nontuberculous side. In some cases careful anamnesis reveals a complaint of pain or soreness in the region of the good kidney, while with accurate physical examination one is surprised at the high percentage of patients who have on the supposedly normal side tenderness in the kidney region and over the ureter at the pelvic brim and in the broad ligament region.

On going back to the records of some of our former tuberculosis patients in whom urograms had been taken on both sides, we were surprised to find the evidences of dilatation on the supposedly normal side, thus demonstrating that much of our routine work in medicine is performed with eyes that perceive but with minds that are slow of apperception.

We see cases of renal tuberculosis in which the history of symptoms, the clinical examination, and the final examination of the removed kidney all suggest that the patient may have had a hydronephrosis or cal-

culus formation, and therefore ureteral stricture, for a long period before the onset of the tuberculosis.

The above considerations led to the deliberate investigation of all cases of renal tuberculosis for the possible presence of bilateral stricture. We have seen only 12 proved renal tuberculosis cases since undertaking this investigation. Two of these patients had bilateral renal tuberculosis and bilateral ureteral stricture, and of course these strictures may have been secondary. One had undergone a left nephrectomy for tuberculosis, and we found advanced renal tuberculosis of the remaining kidney with two ureteral stricture areas and a stone in the upper stricture. The other nine patients had clinical evidence of tuberculosis on one side only, but they all had bilateral stricture.

Twelve cases are far too few from which to draw convincing conclusions, but the fact that careful investigation has demonstrated bilateral stricture in every case (except in the one with the unilateral kidney) is suggestive that this is a field worthy of further study.

We are cognizant of the many pitfalls in the diagnosis of tuberculosis of the kidney, and we have not the space to discuss them here; but for all practical purposes when we can demonstrate that one kidney is doing the better work and that it repeatedly yields a urine free from leucocytes, we may consider this kidney to be nontuberculous.

Space forbids a review of all these cases and we will first present the illustrations with brief notes on three patients to demonstrate some of the interesting problems growing out of a special study of this character. To save space urograms of the tuberculous kidney are omitted.

CASE A.—Fig. 1 is from a patient thirty-eight years of age, who, until a short time before she came to us had always enjoyed exceptional health. In spite of recent complaints she had gained in weight, in the five years previous to admission, from 165 to 180 pounds. There had never been signs or symptoms of lung trouble except for one or two brief attacks of bronchitis. There had been occasional attacks of sore throat and frequent colds, and the tonsils were considerably enlarged and cryptic.

Symptoms probably due to ureteral stricture began about ten years previously as evidenced by an increasing dysmenorrhea accompanied by dull aching and pain in the right side. The youngest of her two children was then five years of age and her menstrual periods had always been normal and free from pains. For several years the symptoms were diagnosed as due to "ovarian trouble," and three years before she came to us she was advised to have an operation for appendicitis. During the past three years there had been about 12 attacks of quite severe right upper quadrant pain accompanied by nausea and vomiting, and followed by a day or two of soreness in the right flank. During the attack, and for twenty-four hours following, voiding was more frequent and slightly painful. There had been no bladder symptoms between attacks until recently. She had never seen blood in the urine. She thinks there had never been fever.

For six months before admission the bladder symptoms had become constant and severe, and she often voided eight times at night. With this constant bladder misery the pain and soreness in the right flank had also become constant and spread across the abdomen.

The patient entered the Woman's Hospital Dispensary in February, 1927, and the resident surgeon, being unable to catheterize the ureters, asked me to see the patient with him on March 1. There was great tenderness over both ureters in the broad ligament region, and palpable infiltration in the region of the right, but the ureter could not be outlined. The bladder showed considerable ulceration suggestive of tuberculosis. The right ureteral orifice region was granular, red and edematous and a catheter would not enter for more than 1 to 2 cm. On subsequent visits we were able to catheterize the left ureter which was found to have dense strictures and the resident finally got this side dilated to a 16 Fr., the patient steadily improving in her general health and the bladder symptoms lessening under the ureteral and local bladder treatment. The bladder urine showed considerable pus but a negative culture. The urine from the left kidney was normal. A half-hour intra-



Fig. 1.—Showing a rather large left kidney shadow with apparently normal pelvis and calices. Left ureteral lumen about normal, but the original film shows two definitely narrowed areas, one in the iliac gland region and one in the juxtavesical region. These x-ray narrowings correspond to two areas of hang obtained by the dilating bulb. Note the rather long liver lappet. Right kidney shadow small. An irregular shadow in lower pole region measuring about 4 cm. by 15 mm., apparently made up of numerous small porous stone shadows. This appearance together with the position relative to the liver aroused suspicion of possible gallstones.

venous phenolsulphonephthalein test showed 33 per cent from the left and about 4 per cent through the bladder from the right kidney. Many slides stained for tubercle bacilli and one guinea pig injection were all negative.

Because of the great improvement under treatment of the left ureteral strictures and because tubercle bacilli could not be demonstrated, we hoped that the case might prove to be one of simple stricture resulting in stone formation in the right kidney; but on the strength of the urinary findings of pus and a negative culture, the appearance of the bladder and the x-ray findings (Fig. 1), suggesting calcareous deposits rather than true stone formation, we diagnosed right renal tuberculosis and I assisted the resident in a nephrectomy on June 16. The opened kidney showed a thin cortex, its upper and middle calices holding large tuberculous abscesses and considerable calcareous material. The patient was followed for seven months with

occasional bladder treatments and she was finally discharged as well January 10, 1928.

CASE B.—Fig. 2 is the urogram of the right side of a girl whose left tuberculous kidney was removed in November, 1925, and whose subsequent history strongly suggests that she belongs in the class of patients who originally have simple bilateral stricture and elusive ulcer of the bladder secondary to a focal infection area.

H. P., aged thirteen years, admitted to the Harriet Lane Home July 25, 1925, because of bladder symptoms of three months' duration, and recent hematuria. There had been but little pain but the patient had nocturnal and diurnal incontinence, the leakage occurring at times as often as every half hour and at times lasting continuously for several minutes. There had been bloody urine on two occasions ten and two days before admission. Examination of heart, lungs, and abdomen



Fig. 2.—Right urogram after left nephrectomy, catheter out. Note the slightly dilated kidney pelvis with dilated upper and lower calices fused with the pelvis. Slightly dilated ureter except in the two stricture areas in the iliac gland and broad ligament regions. Note the large shadow on the left just above the sacrum, calcareous deposits in the lumbar gland region.

negative. "Ragged" tonsils. Tuberculin test 0.10 mg., positive. Catheterized urine: many motile bacteria, many erythrocytes and leucocytes. The patient was transferred to the gynecologic service August 7. Cystoscopy showed almost universal inflammation of the bladder; a culture produced *S. albus* and *B. coli*. Urinary antiseptics by mouth. Frequent rises in temperature.

On October 19 a guinea pig previously inoculated with bladder urine was reported as dead from tuberculosis. On October 27 the patient was cystoscoped under general anesthesia and bilateral ureteral stricture was found, with normal urine from the right and creamy purulent urine from the left kidney. A urogram from the left showed almost universal etching out of the calices, and large calcareous masses in the region of the left lumbar glands.

Left nephrectomy October 31, 1925. Discharged November 24, with normal temperature and marked general improvement but with only slight change in the urinary frequency and incontinence. Placed under the care of a district nurse, who gave instillations twice a week of 1:10,000 bichloride solution, one ounce left

in the bladder. This treatment was continued for about one year, the bladder symptoms gradually lessening and cystoscopy showing marked improvement. In May, 1927, the patient reported that she had no more bladder pain, slept so soundly at night that she did not awaken, but wore a pad for the incontinence. Voided every two to three hours in the day, and had frequent incontinence. Considerable pain at times in the upper right flank. The bladder appeared normal except for a few slightly congested areas in the vertex. We then began occasional dilatation of the right ureter, seeing the patient at intervals of a few months, and by the Christmas holidays, 1928, the ureter was taking bulbs of 5.6 mm. (17 Fr.). The bladder appeared normal except for a tiny area in either side of the vertex which looked typical of elusive ulcer. The wide dilatation of the ureteral strictures having failed to cure her incontinence, we tried thorough fulguration of the ulcer areas under ether anesthesia December 22, 1928. This seemed to improve her condition somewhat but on April 20, 1929, we again began a series of ureteral dilatations and by June 1 had the strictures again taking a 17 Fr. bulb. The incontinence still persisting, we fulgurated a second time on June 20, 1929. This seemed to have no marked effect and we took up the occasional dilatations again in October. In April, 1930, the tonsils were removed and the patient's incontinence soon began to improve. She had 7 ureteral dilatations in the next year and on March 14, 1931, she was discharged as well. At that time she was having no discomfort in the right flank; she sometimes voided once during the night, but never had incontinence. Careful search of the entire bladder showed a normal or slightly scarred condition in the two vertex areas.

The discovery that bilateral simple stricture of the ureter probably antedates tuberculosis of the upper tract in a large proportion of all cases of urinary tuberculosis possibly offers an explanation for many troublesome bladder conditions met with in this group.

For years past urologists have known that after a tuberculous kidney has been removed the accompanying bladder lesion will usually heal within a few months; in a few cases, however, it persists, with serious bladder symptoms, and defies our curative efforts by the usual methods of irrigations, instillations, and local applications.

This persistent lesion is usually found in the vertex of the bladder, and often appears to be quite superficial and innocent, as compared with the far more extensive lesions that may have been present before the nephrectomy. The urine may be quite normal or show only an occasional erythrocyte or leucocyte. In brief, the evidence suggests strongly that in this residual lesion we are dealing with an interstitial cystitis or elusive ulcer rather than with a tuberculous ulceration.

In three cases I have removed these ulcers by operation and have failed to find any evidence of tuberculosis in the excised tissues. Conforming with our experience with elusive ulcer, there may be only one tiny apparently superficial but extremely painful lesion, or several of these small lesions, or one or more large congestion areas may be found in any portion of the bladder. Again one sometimes sees a widespread, dull, red area, resembling parchment, a portion of which may be covered by a dead white area of thickened epithelium quite devoid of vessels, the condition known as leucoplakia vesicae.

Keyes (personal communication) has given considerable study to such conditions as they persist after nephrectomy for tuberculosis, and has come to the conclusion that they should be treated just as one treats the elusive ulcer.

My experience with the frequent association of bilateral ureteral stricture and elusive ulcer of the bladder,<sup>4</sup> leads me to believe that most of these extremely persistent and painful lesions are of the elusive ulcer type (some of them possibly having been present before the onset of the renal tuberculosis), and that they should be treated as such, including careful attention to any distant focus of infection (see Case B).

CASE C.—Fig. 3 shows the right kidney, the urine from which was always negative for pathologic elements until in February, 1932, two years and four months after her left nephrectomy, a guinea pig inoculated with urine from the right kidney died six weeks later of tuberculosis.

M. S., aged fifteen, admitted to the Church Home and Infirmary, October 7, 1929, complaining of pain in the left flank region since her eleventh year. During these five years there had been spells of bladder frequency, but she was often free from urinary distress. Menstruation began about two years ago and was regular for about one year; there was then amenorrhea for six months, after which the periods occurred regularly from March until June this year. There has now been amenorrhea for the past four months.

The patient is a large-framed, emaciated girl. There have never been unusual chest symptoms. There was a suspicious area beneath the angle of the right scapula, and an x-ray film showed evidence of bilateral pulmonary disease. Heart sounds normal, about 100 per minute, temperature reached normal daily, but rose to a peak of from 100° to 103° F. daily during the seventeen days of observation before operation. Blood pressure 100/70. Hb. 68 per cent. R.B.C. 3,910,000. W.B.C. 13,700. Two-hour intramuscular phenolsulphonephthalein 45 per cent. The urine contained a heavy sediment representing half its volume and composed chiefly of pus cells, with many erythrocytes, a large quantity of albumin. Special stains on three occasions were negative for tubercle bacilli, and a guinea pig inoculated with urine from the left kidney failed to show any positive evidence of tuberculosis.

On palpation the left flank contained a mass, apparently the left kidney, reaching about 3 cm. below the umbilical line. We estimated this mass as being about 4 times the size of a normal kidney. The right kidney could be palpated over its lower third and seemed slightly enlarged as if from compensatory hypertrophy. No tenderness over right kidney nor over the right ureter at the pelvic brim. The left ureter in the region of the pelvic brim was tender. Pelvic examination was not made until anesthesia for operation, when the left ureter could be traced from the bladder almost to the pelvic brim as a thickened mass larger than a lead pencil. The right ureter could be traced for about 4 cm. beyond the bladder as a thickened cord the size of a slate pencil.

The bladder, when filled to discomfort, was catheterized and 110 c.c. were obtained. Cystoscopy revealed almost universal ulceration of the bladder. The mucosa of the base and trigonal region was so red and edematous that the ureteral orifices could be found only by probing with the metal searcher. Neither side could be catheterized. After a week of daily irrigations the bladder had improved somewhat. The left ureteral orifice was seen to be secreting a thick purulent material. The left side was catheterized and the urine was so purulent that it ran very slowly through the No. 8 catheter. Urograms showed all the lobules deeply excavated. In spite of the failure to find tubercle bacilli, the evidences of lung involvement, and of a

practically destroyed left kidney, with a negative culture from the purulent urine, were such as to prompt us to do a left nephrectomy. The fact that a catheter would not enter the right ureter, together with the findings on palpation during anesthesia, made us suspect that the right kidney might also be involved but its two-hour phenol-sulphonephthalein output of 45 per cent showed that it was capable of sustaining fair health, and we felt confident of improving its working capacity by later ureteral dilatation.

Left nephrectomy October 24, 1929, removing a kidney weighing 2.75 pounds, 1026 gm., or about 7 times the normal. The temperature chart for twenty-eight days until the patient's dismissal showed an elevation to 99° F. on two occasions. At our request the patient returned in February, 1930, four months after operation. She weighed 123 pounds, a gain of 33 pounds. The bladder had improved markedly in appearance, there being many normal-looking areas. The right ureter was entered with much difficulty due to dense infiltration in the lower ureter. The kidney urine was normal and negative for tubercle bacilli on slide stains and a guinea pig test. The following summary gives some idea of the progress in the more than two years after the left nephrectomy.

	OCT. 1929	FEB. 1930	FEB. 1931	MAR. 1931	JAN. 1932	FEB. 1932
Weight, pounds	90	123	150	153		
Blood pressure	100/70	126/90			122/78	
Bladder capacity in c.c.	110	260	270	330		
Right kidney ca- pacity in c.c.		30	28		24	
Two-hour phenolsul- phonephthalein per cent	45	51			55	60

In September, 1930, the patient had several hemorrhages from the lungs over a period of four days, this being the only active clinical sign of pulmonary disease she has had.

As before stated, there had been 3 stained slide examinations before operation with negative results. Two of these (October 8 and 14) were from the bladder urine and one (October 14) from the left kidney urine. A guinea pig inoculated with the left kidney urine on October 14 was autopsied on November 22, and showed a suppurating gland in the groin, but no other evidence of tuberculosis. A smear from the suppurating gland and stained sections of the gland were negative for tubercle bacilli.

After the operation stained slides were made from the bladder urine on February 7, 1930, and from the right kidney urine on February 7 and February 17, 1930, all being negative. Guinea pigs were inoculated after operation with the bladder urine on February 7, 1930, and on February 2, 1931. The latter animal was autopsied March 16, 1931, and was positive for tuberculosis. Urine from the right kidney was inoculated February 17, 1931, and February 24, 1932. The latter animal was autopsied April 7, 1932, and was tuberculous. During the two years the urine from the right kidney was examined on 6 occasions, but leucocytes were never found. Serious bladder symptoms had always been surprisingly absent even on the first visit when a normal area of mucosa could not be seen, and the capacity was only 110 c.c. On the last visit in February, 1932, the patient reported voiding only once or twice at night and at three- to four-hour intervals in the day. The mucosa still showed general congestion with many areas of brilliant redness. Some of these areas were partially covered by a fibrinous-like coating, but this could not be re-





Fig. 3.—Urogram April 22, 1931, 28 c.c. NaI, catheter out. Note well filled lower half of pelvis with clean-cut outlines. Other urograms of entire kidney show similar sharp outlines. Partially filled ureter showing convolutions. Narrow lumen in bladder wall region. Note the unusual picture of a cone-shaped spurt of NaI from the ureteral orifice.

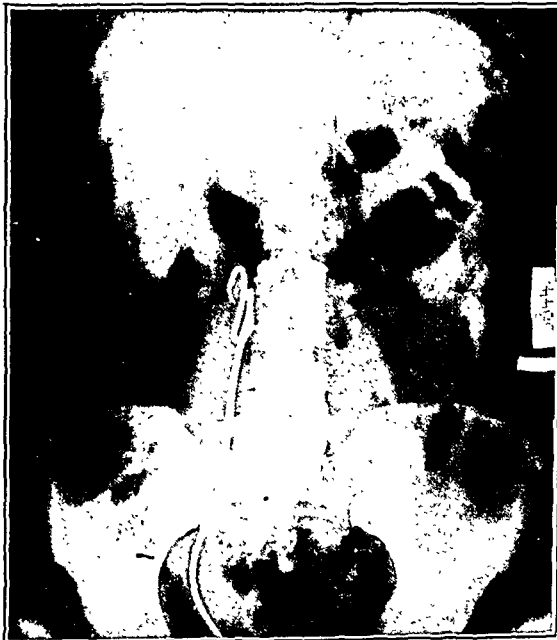


Fig. 4.—Case 1. Plain plate showing tip of x-ray catheter curved up over a stone the size of a navy bean located beside the third lumbar interspace. Note that the patient has six lumbar vertebrae, and that there is fusion of the third and fourth. The history suggests that the patient had an active invasion of the spine when at school at fifteen years of age, the symptoms subsiding completely after five months of rest.

moved by brushing it with a dry cotton pledget, and I interpreted this as a leucoplakic process of healing.

#### THERAPEUTICS

What therapeutic evidence have we that the restoration of better urinary drainage by thorough dilatation of ureteral stricture may favorably influence the progress of renal tuberculosis?

Since the development of this new conception of the etiology of renal tuberculosis, we have had the opportunity to make use of it therapeutically in only 6 cases. The elapsed time has been too short and the number of cases far too few to justify conclusions of any kind, but our



Fig. 5.—Case 1. Urogram after the stone had passed, showing pelvis of 50 c.c. capacity, stricture area in the broad ligament region with moderate dilatation of the pelvic ureter, and wide dilatation of the abdominal ureter which is incompletely filled. The original film shows plainly a narrow area opposite the fourth lumbar from which the stone was dislodged after several dilatations.

experiences to date suggest that further critical studies should be made in this important field.

CASE 1.—(Figs. 4 and 5.) In the case of a patient thirty years of age, who had lost one tuberculous kidney by nephrectomy, we were forced into this drainage treatment as the only method available for helping the remaining tuberculous kidney. She had a stricture in the broad ligament region and a high stricture containing a stone at a point opposite the third lumbar vertebra. We were able to dilate both these strictures and get a spontaneous passage of the ureteral stone.

On admission this patient's hemoglobin was 65 per cent, the intravenous phenol-sulphonephthalein test showed, first hour, 110 c.c. 8 per cent, second hour, 550 c.c. 42 per cent, and the nonprotein nitrogen was 54 mg. per cent. During four months of treatment in which the ureteral dilatations were carried up to 5.6 mm. (17 Fr.), the patient had occasional attacks of discomfort in the right flank, accompanied

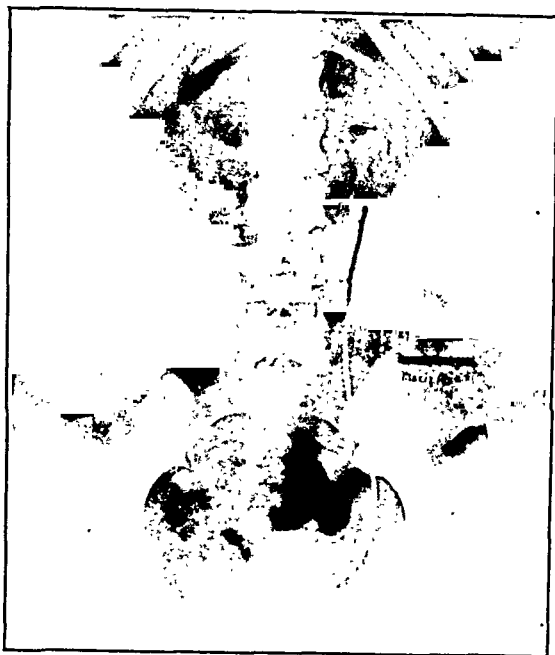


Fig. 6.—Case 2. At the first investigation the catheter tip was obstructed in passing through the broad ligament region, and this film shows the tip permanently stopped at about the level of the lower pole of the left kidney. Two tiny calcareous particles appear in the upper portion of the kidney.



Fig. 7.—Case 2. The catheter has been withdrawn until its bulb, 10 cm. back from the tip, is hanging in the broad ligament region about 3 cm. above the bladder. Note the slight dilatation of the ureter from this point to the kidney, except for two areas of filling defect near the kidney, and that no urogram solution gets through into the pelvis. In the original film the filling defects in the upper ureter show an irregular feathery or nodular outline suggesting neoplasm or tuberculosis.

by headache and nausea, showing that her stricture areas still narrowed down at times and interfered with drainage, and that her tenure of life was not at all promising. These attacks were particularly prone to occur with the menstrual periods. Her general health and ability to take moderate exercise improved, but she died thirteen months after she left our care.

CASE 2.—(Figs. 6, 7 and 8.) In a second case with bilateral renal involvement we probably saw the patient too late to give the drainage method a fair trial. It was evident that both kidneys were badly diseased, but the showing of a normal blood chemistry and a two-hour intravenous phenolsulphonephthalein output of first hour 45 per cent and second hour 15 per cent, and a half-hour differential test showing,

	APPEARANCE TIME	AMOUNT	PER CENT
Left kidney (catheter)	6 minutes	135 c.c.	30
Right kidney (bladder)	15 minutes	44 c.c.	2



Fig. 8.—Case 2. Taken one month after Figs. 6 and 7, showing that the tip of a No. 7 catheter with an 11 Fr. bulb placed near the tip had gone well over into the kidney. The kidney held 10 c.c. of urogram solution. The urogram suggests slight hydronephrosis with slight reflux of solution down the ureter for a distance of 4 cm. (Compare upper ureter in Fig. 7.) Deformity of all calices, the uppermost calyx being clubbed and its neck almost cut off, suggesting an abscess cavity in the upper pole. Two others of the upper calices almost obliterated. Two middle calices showing tiny cups and thin necks almost obliterated. The lower calices dilated and merging broadly with the pelvis. On withdrawal of the catheter the small bulb near the tip had a rather firm hang near the kidney in two areas, at about 26 cm. and 24 cm. from the outside and in a third area near the bladder (see Fig. 7).

We felt that improved ureteral drainage offered the only possible hope for improvement.

After inadequate ureteral dilatation had been established in the spring of 1927, the patient went north for the summer vacation. In the fall her husband wrote that she had gained 13 pounds in weight and that her general health seemed improved. They had decided to avoid the long trips to Baltimore and to have further treatment by a home surgeon in New York City. After the usual investigation and a confirmation of the bilateral tuberculosis, it was decided that her general and renal conditions did not justify further active interference and the patient died in January, 1928.



Fig. 9.—Case 3. Tuberculous pyonephrosis right kidney. Note the stricture area about 3 cm. above the bladder and the large ureter and kidney holding 50 c.c. Note apparent obliteration of the uppermost calyx and slight filling defect of the lower calyx.



Fig. 10.—Case 3. Left kidney pelvis and calices slightly smaller than normal, holding 5 c.c. The bulb repeatedly demonstrated 5 stricture areas in beadlike sequence, the highest being 16 cm. above the external urethral orifice. Note the upper filling defect opposite the lumbosacral joint, and three filling defects in the pelvic ureter.

CASE 3.—(Figs. 9 and 10.) In a third case our preliminary investigations made us quite certain that we were dealing with a tuberculosis of the right kidney, but the miraculous improvement in the local and general conditions of the patient after a few ureteral dilatations forced us to question our original diagnosis. Miss B., aged twenty-one years, was referred by Dr. Julius Friedenwald in March, 1926. There had been moderate attacks of pain in the right upper flank region on five occasions in the previous two years. The patient's mother had died of tuberculosis, and the patient was of the tall frail type, but quite athletic in her pursuits.

Physical examination and x-ray of the thorax were negative. The patient had not been conscious of her side between attacks and there had never been urinary frequency. The bladder urine showed about one-fifth of the volume as a heavy purulent deposit, and a trace of albumin, but was negative to culture. Palpation revealed slight tenderness over the lower pole of the right kidney and great tenderness over both ureters in the broad ligament regions, the left seemingly showing more tenderness than the right. On cystoscopy the bladder everywhere appeared to be normal except in the trigonal area, which was deeply red and congested, and the right mons ureteris was "puffy and edematous, suggesting a tuberculous condition."

Further investigation revealed bilateral ureteral stricture with a 50 c.c. pyonephrotic kidney on the right, the left kidney pelvis being smaller than normal, holding only 5 c.c., and yielding normal urine. The half-hour intravenous phenol-sulphonephthalein test, after both sides had been well dilated, showed an output of 20 per cent on the right and 45 per cent on the left.

Under dilatations the patient gained 20 pounds in weight in the first two months and at the end of four months the following note was made on the urinalysis: "Urine catheterized from the bladder, after standing six hours, looks like clear water, shows no visible precipitate; pipetted and centrifuged. A slide preparation shows 1 to 4 leucocytes in a high-power field, a few epithelial cells, no erythrocytes, no casts; there was no albumin."

Fifteen months later the patient again developed symptoms, and the bladder urine was found to contain about half as much pus by volume as on the first investigation. I was unable to pass even the finest whalebone filiform through the stricture area in the right broad ligament region. For the first time we demonstrated tubercle bacilli by guinea pig test, and right nephrectomy was done two years after the first consultation.

This case illustrates the difficulties sometimes encountered in making a positive diagnosis of tuberculosis of the urinary tract. During the two years of observation and treatment this patient had been in two hospitals on ten different visits, and because of the original urinary and cystoscopic findings I had suggested the likelihood of finding tubercle bacilli. In each of her admissions at least one and sometimes several examinations were made of the urine from the bladder or from the right kidney. Either one or two guinea pigs were inoculated on four different occasions and the sixth was the first to die of tuberculosis.

One of the strongest arguments against the right kidney being tuberculous was the prompt manner in which the urine cleared up when we first established good drainage. Before the experience with this case I held the view that if a pyonephrosis or an infected hydronephrosis does not promptly clear up with the establishment of good ureteral drainage, we should exert every effort to demonstrate tubercle bacilli, even though the urine on culture yields a pyogenic organism, but here we have

a case in which drainage resulted in such rapid clearing of the urine that we were almost diverted from any further search for tuberculosis.

The two following cases, illustrated by Figs. 11 to 14, seemed to offer a fair test for the drainage method of treatment, but one patient has had the tuberculous kidney removed and the other has been advised to follow this course. Each presented bilateral ureteral stricture, and unilateral renal tuberculosis with approximately equal and normal bilateral functional tests. Each of them showed gain in weight and improvement in general health as an early result of the bilateral drainage.\*

The following case represents an apparent cure of a bilateral renal tuberculosis, following no other measures than the establishment of good ureteral drainage. The patient had a definite history of right renal attacks for five years; with one attack on the left side, and the passage of a ureteral stone, two years previously. These phenomena are not uncommon in cases of simple ureteral stricture. The x-rays revealed advanced bilateral hydronephrosis, also a common sequel of stricture; but the flat film showed multiple deposits in the calices which led to the discovery of tubercle bacilli in abundance in spite of an almost perfectly normal urinalysis.

CASE 6.—(Figs. 15, 16, and 17.) Mrs. M. L., aged thirty-five, para iii, first admitted to the Johns Hopkins Medical Service October 23, 1919, because of a severe attack of pain in the right upper quadrant and intense jaundice. Six attacks of similar pain without jaundice in the previous eight months. On admission she was also suffering with a marked Vincent's angina and a right parotitis. Tonsillitis attacks over a period of many years, and diphtheria in 1909. Two dental abscesses four years previously.

After subsidence of the acute condition about the mouth, parotid and gall bladder regions the patient was transferred to the surgical service on December 5, and on December 10 a diseased appendix and gall bladder were removed. Gall stones were not found in the bladder or ducts, but the gall bladder had a deep hour-glass constriction in its midportion and dense adhesions to the duodenum. Drainage to the common duct was instituted by means of a small rubber tube sutured into the cystic duct. The patient made a rapid recovery and first entered the gynecologic dispensary about six and a half years later, or in June, 1926. About one year after the operation she began having attacks characterized by an uneasy feeling in the mid-epigastrium which disappeared after massage followed by belching. Later severe attacks began with pain in the right posterior flank region, working forward into the epigastrium, and ending in marked nausea and vomiting. These attacks formerly occurred at intervals of about five or six months but in the past year they had come at about monthly intervals and there had been 3 attacks in the past month. Hypodermics of morphine were frequently necessary in these attacks. The urinalysis was negative except for a few erythrocytes and a large amount of amorphous débris.

About two years before admission she had had a similar severe attack on the left side and a small stone had been passed. She entered a neighboring hospital where catheters were passed and x-rays taken, and she was more comfortable for about six months. At the present time she has no marked bladder symptoms, but she

\*To economize space the detailed histories of Cases 4 and 5, Figs. 11 to 14, are omitted in the *JOURNAL* but will appear in the reprints to be furnished by the author on request from those especially interested in this subject.

voids about twice at night, and at two-hour intervals in the day. With the attacks she often voids at hourly intervals.

Cystoscopy revealed an apparently normal bladder except for numerous glistening vesicles scattered over the posterior wall, and a red edematous condition of the



Fig. 15.—Case 6. Urogram, right side, 50 c.c. NaI. Deformity of calices, with suggestion of filling defect in middle and lower calices. Calcareous deposits outlining calices of left kidney. Phleboliths or calcified glands in both broad ligament regions.



Fig. 16.—Case 6. Flat film, taken five years after Fig. 15, showing two stones of irregular outline in the lower end of the left ureter.

trigoneum and around the ureteral orifices. The latter suggested tuberculosis, but the absence of pus after a history of attacks over a five-year period was strongly against such a diagnosis. In nearly all later examinations we were able to demonstrate



an occasional pus cell in the centrifuged urine from the bladder and from either kidney. Further investigations in the succeeding weeks revealed bilateral ureteral stricture and bilateral hydronephrosis, the right kidney holding 50 c.c. (Fig. 15) and the left 26 c.c.

The patient was a large-framed woman, weighing 150 pounds. General physical examination was negative except for enlarged, angry-looking tonsils, a suspicious dental condition and tenderness on palpation of the right kidney and over both ureters at the pelvic brim and broad ligament regions. A hard nodule was palpated in the right broad ligament region and interpreted as being a phlebolith.

The plain x-rays revealed numerous tiny shadows in the region of practically all the calices. With this evidence a search was made and tubercle bacilli were found in abundance in the catheterized bladder urine. Guinea pigs inoculated on September



Fig. 17.—Case 6. The No. 9 whistle-tip x-ray catheter has displaced both ureteral stones up into the kidney pelvis.

14 from the bladder and left kidney urines, on September 23 from the right kidney urine, and on September 26 from the left kidney all died from tuberculosis.

The ureteral dilatations were carried up to a 6 mm. (18 Fr.) dilatation and the patient rapidly improved in general health, her only complaint being that she was "getting too fat." Her weight increased from 150 to 168 pounds in the first ten months of treatment, and to 178 pounds in the next year. In January, 1927, we found that an irregular angular stone had lodged in the right ureter. This was probably caused by the coalescence of smaller calculi which had become freed from the deposits in the calices. Being irregular in outline it was difficult to dislodge from the stricture area in the right broad ligament region, but its irregularity probably also allowed free drainage of urine, for the patient was not inconvenienced by it. This stone passed spontaneously in March, 1927. Negative guinea pig inoculations were made as follows: R. kidney xii, 10, 1927; ii, 14, 1928; ii, 14, 1929; iii, 5, 1929; L. kidney xii, 29, 1927; iv, 5, 1928; ii, 29, 1929; vi, 26, 1929. Many stains were made from the bladder and kidney urines during the three years from June, 1926, to June, 1929, the specimens often being centrifuged for a long period and examined

most carefully, and after the first six months of her treatment tubercle bacilli could not be demonstrated.

In spite of our urging that the patient report at six-month intervals she was so well that we did not see her from June, 1929, until April 2, 1931. At that time she returned because of a dull pain in the left side. Investigation revealed two stones in the left ureter, one about 2 cm. and the other 1 cm. long (Fig. 16). These stones appeared irregular in outline, and after our experience with the prolonged difficulties of dislodging the conglomerate stone from the right ureter in 1927, we decided to remove these left ureteral stones by operation. These stones were migratory and could be displaced upward into the kidney by the whistle-tip No. 9 x-ray catheter (Fig. 17), but in spite of a dilatation up to a 4.6 mm. (14 Fr.) the stricture areas would not allow the stones to pass. Unlike the one on the right side, these stones caused enough blockage of the ureter to bring on renal pain and fever, the chief factor in the decision for operation. This was done June 11 through a left McBurney extraperitoneal incision, and we had considerable difficulty in dragging all the stone material up from the broad ligament region. Like the former stone on the right side, these stones on the left were apparently conglomerates, made up of fused particles coming down from the calices. After their removal, dilating bougies up to a 15 Fr. were passed through the stricture in the broad ligament region, and the ureter was left open for free drainage in case the trauma of the operation should result in edema and temporary closure of the stricture area. In one week the urinary drainage had ceased and the cigarette drains down to the region of the ureter were removed. Before the operation guinea pigs were inoculated from the urine from each kidney and both were negative for tuberculosis. Slides were stained on numerous occasions from specimens from the bladder and both kidneys, and all were negative.

The patient was discharged in good condition at the end of four weeks. Three weeks later, or on July 31, 1931, she was brought to the hospital at night in a moribund condition after an apparent history of intestinal obstruction of one week's duration. She was taken directly to the operating room in the hope that intravenous fluids might place her in condition for an exploratory incision under local anesthesia. The abdomen was greatly distended and there was an indefinite mass in the right upper quadrant. While taking the intravenous glucose solution and before an incision could be made the patient died.

Our resident gained permission to make an exploratory incision which revealed 2 or 3 feet of black jejunum, the infarct being due to a volvulus of the mesentery. Unfortunately permission to remove the kidneys was refused and a unique opportunity was missed to ascertain whether after five years of good drainage there had been actual healing of the tuberculous process.

You will note in the program synopsis of my paper that I proposed to report one case of unilateral renal tuberculosis as cured. Since digging into the records of this patient I am disappointed in having to drop her from our tuberculosis list. These records furnish such a striking example of the care one must use in arriving at a diagnosis of renal tuberculosis, and show so well the rôle of ureteral stricture in causing many of our common urinary tract complaints that a brief summary of the facts are pertinent.

In 1927 one of our resident gynecologists showed me the urogram (Fig. 18) of a patient he had been treating for supposed right renal tuberculosis and gave me from memory the following data. Tubercle

bacilli had been found in abundance in the urines from the bladder and right kidney and guinea pigs inoculated from these sources had died of tuberculosis.

After six months dispensary treatment of bilateral ureteral stricture the patient was symptom-free, the urine was normal, careful slide and guinea pig examinations for tubercle bacilli were negative, and the resident considered the case as one of recovery from renal tuberculosis. The facts seem to be as follows:

CASE 7.—Mrs. E. H., aged twenty-seven, para iv, was admitted to the gynecologic service July 15, 1926, complaining chiefly of pain in the right flank, hematuria, and acute arthritis of the metacarpophalangeal joint of the right index finger. Seven years previously in the third month of her third pregnancy the patient had had a



Fig. 18.—Case 7. Right urogram of patient with bilateral ureteral stricture erroneously diagnosed as right renal tuberculosis.

spell of great urgency and frequency of voiding, with hematuria. This had soon cleared spontaneously and there had been no further trouble in that or the subsequent pregnancy. Since that first attack there had been intermittent spells of frequency but no bleeding until the present illness. For the past six months the patient had grown progressively weaker. Has had nervous and crying spells. At times sudden slight fever and in the past few weeks, night sweats. Spells of dry cough without hemoptysis. In the last few months occasional pains in the upper chest, considerable headache. In 1917 "pneumonia and influenza." Occasional mild sore throat since. Two months ago began to have intermittent attacks of sharp pain in the right flank region, and these have been more severe and persistent since an attack of tonsillitis two weeks ago. For the past week there has been much urgency and urinary frequency, and the passage of bloody urine. The acute arthritis of the right hand began at about the same time, together with fever. The catheterized bladder specimen showed many erythrocytes and leucocytes and a culture of bacillus

coli. Because of the history suggesting an early pulmonary tuberculosis, and a more recent tonsillitis followed by possible acute hematogenous nephritis, and because the patient's chief complaints on admission were centered on the acute and painful arthritis, she was referred for study to the medical service.

Evidences of chest tuberculosis were absent. Blood cultures and the Wassermann test were negative. A *Streptococcus hemolyticus* was recovered from the right tonsil. The urine was carefully centrifuged on four successive days, and on three of these acid-fast bacilli were found. The note on the last examination states, "A voided specimen was then treated by the method of Petroff and after 50 per cent alcoholic dilution was centrifuged at high speed for two hours. Sediment then stained by the method of Ziehl-Nielsen and a clump of three acid-alcohol-fast bacilli were seen. These were examined by several members of the medical house staff, who agree that morphologically they are Koch's bacilli."

After nineteen days in the hospital the patient's arthritis had subsided, her temperature was normal, and the urine was free from pus and blood. She was then referred back to the gynecologic service for further investigation for a possible renal tuberculosis. Bilateral ureteral stricture was found, the urine from each kidney being normal. Tubercle bacilli were not found on stained slides after the patient's transfer to the gynecologic side.

During July, August, and September guinea pigs were inoculated as follows: four times from the bladder urine, and four times from the kidney urines, twice from each side. Evidences of tuberculosis were not found in any of these eight pigs. One naturally wonders on what basis the case was reported to me as one of tuberculosis. On investigation of the medical records I find that four examinations were made of the bladder urine, one of a catheterized specimen, in which tubercle bacilli were not found, and three on voided specimens, in all of which acid-fast bacilli were found. The patient was found to have an inflammation of Skene's glands, the pus from this source showing intracellular diplococci. These facts seem to point to the one conclusion that the acid-fast organisms originally identified as tubercle bacilli should have been called smegma bacilli. As further evidence that this patient's urinary tract troubles originated from a ureteral stricture condition, I found on the recent review of her records that she remained well nearly four years, and then returned in 1930 with many of her old symptoms such as malaise, extreme nervousness, night sweats, pain in the right flank, fever, and frequency of voiding. After a few dilatations these symptoms ceased.

This patient undoubtedly represents one of that great group seen in urology in whom the pathologic conditions in the kidney and general ill health are largely dependent on inadequate renal drainage secondary to ureteral stricture. It would be useless to speculate on what proportion of nephrectomies for supposed tuberculosis belong in this group. Fortunately, the number grows rapidly less since surgeons are now making use of the diagnostic and therapeutic methods made possible by a knowledge of ureteral stricture.

Is it wise to suggest the possibility of any other method of dealing with renal tuberculosis than by nephrectomy, which we have found so promptly effectual in such a large proportion of our cases?

It is perhaps fortunate that this first report on the drainage method makes such a poor showing in actual results that no one should be carried away by an enthusiasm which might lead to such an indiscriminate use of the method as to work harm to the patient.

Our present diagnostic methods in urology, including the microscopic study of the separate urines from each kidney, the differential functional tests, the x-ray studies, and the bulb studies of the ureteral condition, are now so perfected that we can arrive at a fairly accurate estimate of the condition of each kidney. For the present time at least, and until we have had far greater experience, this drainage method should not be tried except in those patients whose renal lesion seems to be of moderate extent and the affected kidney of good working capacity.

Curiously enough, and as a striking example of the futility of dogmatic attitudes in dealing with renal tuberculosis, the very patients on whom we obtained the most striking results in the above list of six cases treated by drainage, were two (Cases 3 and 6) in whom our diagnostic yardsticks indicated that we were dealing with a widespread and advanced renal involvement; whereas Cases 4 and 5, apparently showing slight involvement, were the most disappointing in ultimate results.

In Cases 4 and 5 the patients came from a midwestern state and could be treated only at intervals of about six months. In the future I would undertake the drainage methods only in patients who live near enough to be seen conveniently at any time.

We know that tuberculosis heals in various portions of the body, and theoretically the kidney, with its rich circulation and ideal methods of irrigation, should offer an unusual area for spontaneous healing. If, as our experience seems to indicate, ureteral stricture is the chief factor of interference with the natural irrigation properties of the kidney, we may look for healing in a certain number of cases if we can restore good drainage. We are certain that in dealing with chronic pyogenic infections of the kidney there has been no other healing method to compare with that of establishing good drainage through dilatation of the ureteral strictures. In renal tuberculosis any area of ureteral obstruction may be the site of tuberculosis and as such it offers a more serious problem in treatment than simple stricture. We know that bladder tuberculosis often heals, why should ureteral tuberculosis not do so?

This report is justified if the general adoption of bilateral ureteral dilatation is limited to patients who have bilateral renal tuberculosis. It is generally agreed that surgery is contraindicated in such cases except when one kidney is practically destroyed and is the source of severe toxic symptoms, while the other kidney is doing fairly good work. In such cases bilateral ureteral drainage, if feasible, before operation, will probably improve the patient's condition and render operation less dangerous, and the later careful attention to ureteral drainage on the remaining side should do much to reduce discomfort and prolong life. A friend, who had undoubted bilateral renal tuberculosis and had had the more damaged kidney removed, lived a most active and highly useful life for eighteen years after the nephrectomy. We have seen several bilateral cases in which, without drainage treatment, the patients have surprised

us by their comparative activity and length of life, and in the future we shall undoubtedly be able to alleviate such conditions.

Case 6 affords a striking example of what may be accomplished in a patient showing every evidence of widespread involvement of both kidneys. In the early films nearly every calyx area was spotted with calcareous deposits presumably indicating universal ulceration. Five years later, in spite of the acute renal inflammation caused by partial block of ureteral stones, we were unable to demonstrate tubercle bacilli by stain or guinea pig inoculation.

Another group in which the method of drainage cannot be criticized is illustrated by Case 1, and includes those patients who have lost one kidney from any cause and present with a tuberculous condition of the solitary kidney.

In some patients of advanced age, especially if there be other contra-indications to operation, this method of drainage may prove of distinct palliative value. This would apply particularly to those who are fortunate enough to have escaped serious bladder symptoms. Case A illustrates that, with bladder symptoms of severe grade, the dilatation of the non-tuberculous side may greatly alleviate these symptoms, even before the removal of the tuberculous kidney. In several previous publications I have shown that simple ureteral stricture is one of the most common causes of serious bladder symptoms, even inducing complete incontinence of urine; and one of the most satisfactory discoveries in the study of cases with elusive ulcer of the bladder has been that in a considerable proportion of those who have both ureteral stricture and elusive ulcer, the thorough dilatation of the ureters results in such reduction of the bladder symptoms that we are not called upon to treat the bladder lesion.

In certain cases in which tuberculosis is strongly suspected, we are justified in continuing the drainage treatment until we can prove the presence of tuberculosis, providing the patients are answering favorably to the treatment as in Case 3.

In the apparently early unilateral cases we have probably lost no ground by the delay of a few months in doing a nephrectomy, should this become necessary because of a progression rather than a regression of the tuberculous process.

The strongest argument against the method is the danger of carrying infection to the nontuberculous side in making repeated dilations of the simple ureteral stricture on this side. In my first paper on renal tuberculosis twenty-eight years ago, I strongly condemned the passage of a plain catheter to the supposedly healthy side even for the purpose of more accurate diagnosis, and many writers since have emphasized this danger. I know of no one who has seen definite evidence of this transplanting of the disease, but the theoretical dangers seem so great that we should use the utmost precaution in dealing with the nontuberculous side. It may be fairly questioned whether tubercu-

losis was carried from a diseased bladder to the kidney in our Case C. We failed to catheterize the good side in the one attempt before operation. Tuberculosis was not proved until the immense left kidney was removed. Four months later we began dilatation of the right ureter, and in two years of intermittent treatments leucocytes were never found in the kidney specimen. A guinea pig inoculated with bladder urine one year and four months after operation died of tuberculosis. A guinea pig inoculated with the right kidney urine two years and four months after operation died of tuberculosis. Was this infection carried to the kidney from a tuberculous bladder, or were both of these pigs killed with tubercle bacilli which temporarily were being secreted through the blood stream from the known lesion in the lung?

If in the individual case evidences of stricture are wanting on the better side, no further treatment is indicated. If stricture and evidence of stasis are present on the nontuberculous side, our present knowledge leads us to believe that we must at least weigh the danger of blood stream infection of that side, because of the stasis, against the danger of even careful manipulations through the bladder in the effort to dilate the stricture, relieve the stasis, and restore a more normal renal circulation. While thus relieving the local situation, we may be adding tremendously to the patient's general powers of resistance by incidentally relieving headache, gastrointestinal and bladder symptoms, all of which may be partially due to the stasis and absorption of toxic products incident to the stricture on the supposedly normal side. The gain in weight and general well-being was a striking phenomenon in the last four of the above six verified cases, or in those who had a fair trial of the drainage method.

#### CONCLUSION

I would urge that, in the absence of contraindications to operation, early nephrectomy is the only treatment in those cases in which preliminary studies reveal a badly involved tuberculous kidney on one side only. This was done in 6 of our 12 cases and all these women are living in apparently good health, but I attribute this good condition in part to the treatment of establishing good drainage for the remaining kidney, as illustrated by our Cases A, B, and C.

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## THE DIAGNOSIS OF PERITUBAL ADHESIONS AND TUBAL STRICTURES BY UTEROTUBAL INSUFFLATION\*

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**S**TRICTURES of the fallopian tubes may be slight or almost occlusive. In any case their presence is of importance as a cause of sterility. They may be due to partial agglutination of the folds of the tubal mucosa or to adhesions and angulations with so little thickening, as not to be palpable. Firmer adhesions and distortions which are not associated with distention of the tube may also escape detection by bimanual examination. It is with these nonpalpable lesions that the present paper is concerned.

As bougies are out of the question unless a laparotomy is performed, some other method must be sought which will enable us to diagnose such permeable strictures clinically. Such a diagnosis is possible with the use of uterotubal insufflation combined with the kymograph.

An apparatus has been described which supplies and regulates the flow of carbon dioxide gas, combined with a syphonmeter (volumeter), a manometer, and a kymograph upon which the pressures reached during the insufflation are recorded (Fig. 1).

It has been found that normal tubes not only allow the gas to pass through them freely under relatively low pressures but in addition oscillations are observed that have a rhythmic character (Fig. 2-a). These oscillations have been demonstrated to be due to rhythmic contractions of the fallopian tubes. They show only slight variations in frequency per minute in the postmenstrual interval when the test is most suitably carried out.

If the tubes are sealed, the pressure oscillations are absent. As a rule sealed tubes can tolerate a pressure of 200 mm. Hg which has been selected as the high limit of safety to which the tube may be subjected during the insufflation (Fig. 2-b). This is arbitrary but holds for most cases. If higher pressures are used and the gas is found to have entered the peritoneal cavity it indicates that we are dealing with very high grade strictures or that the closed tubes have ruptured. Spastic tubes may resist high pressures but when the spasm is overcome rhythmical contractions are the rule (Fig. 2-c).

High grade strictures have almost the same significance as complete closure of the tubes. In very rare exceptions, nature (with or without the aid of insufflation or lipiodol injection) may succeed in surmounting the difficulty and pregnancy may take place. Observers have recorded occurrences of this kind and I have met with a few instances.

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\*Read at a meeting of the New York Obstetrical Society, January 12, 1932.



Whether the stricture is relatively mild or extremely tight, the type of curve is more or less the same, higher pressures accompanying the tighter strictures. In normal tubes there is a sharp rise and fall in pressure with typical oscillations varying in depth between 15 to 30 or more

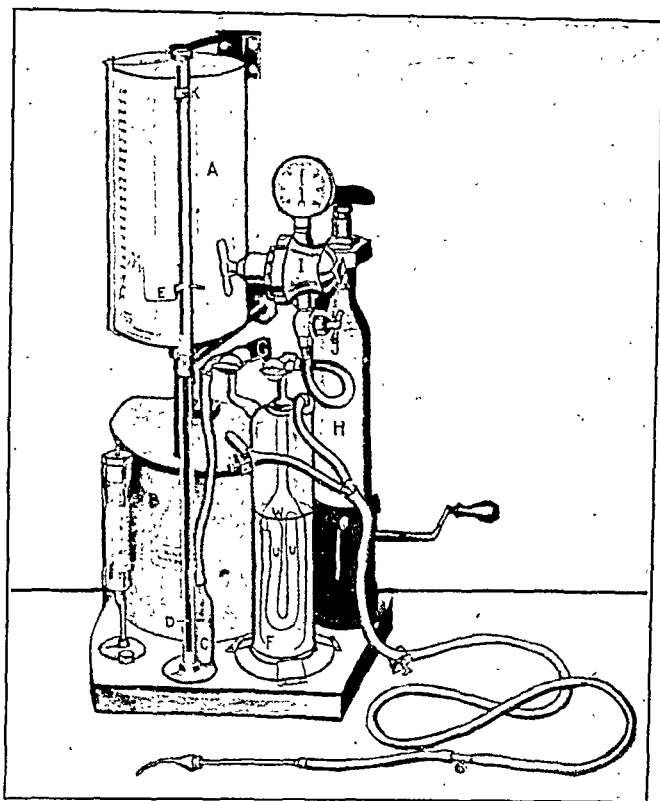


Fig. 1.—Apparatus for uterotubal insufflation. *A*, kymographic drum; *B*, the spring motor; *C*, mercury manometer with float (*D*), and ink writing pen (*E*); *F*, glass syphonmeter with two stopcocks (*G*) closed, to prevent the solution from spilling, when the apparatus is carried in the horizontal position in its case; *H*, carbon dioxide cylinder; *I*, pressure reducing valve with pressure gauge; *J*, needle valve for fine adjustment of the gas flow; *K*, safety (blow off) valve.

mm. Hg (Fig. 2-*a*). In the case of strictures the rise of pressure is more curved, the descent is more gradual and there is apt to be complete absence of typical oscillations. The absence of oscillations indicating loss of tubal contractions is constant in the high grade strictures where the initial pressure rise is well above 100 mm. Hg, most often between 150 and 200 mm. Hg. In the relatively mild strictures due to circumscrib-

ing adhesions there may be noted atypical oscillations which are very shallow and arrhythmic. When the tube is bound down lightly as by filmy adhesions which do not distort it, there may be the slightest variation from the normal. It may be mentioned in this connection that in prolonged amenorrhea tubal contractions may be absent.

If the tube is bound down by very firm adhesions on all sides so that its motions are impaired, the rhythmic contractions are not seen although the pressure levels may not exceed the normal.

There also appears to be a marked difference due to the location of the stricture, i. e., at the isthmus or the ampulla. Isthmic stenosis is more apt to block tubal peristalsis and interfere with rhythmic contractions to a greater degree than stenosis situated at the ampulla or the fimbria.

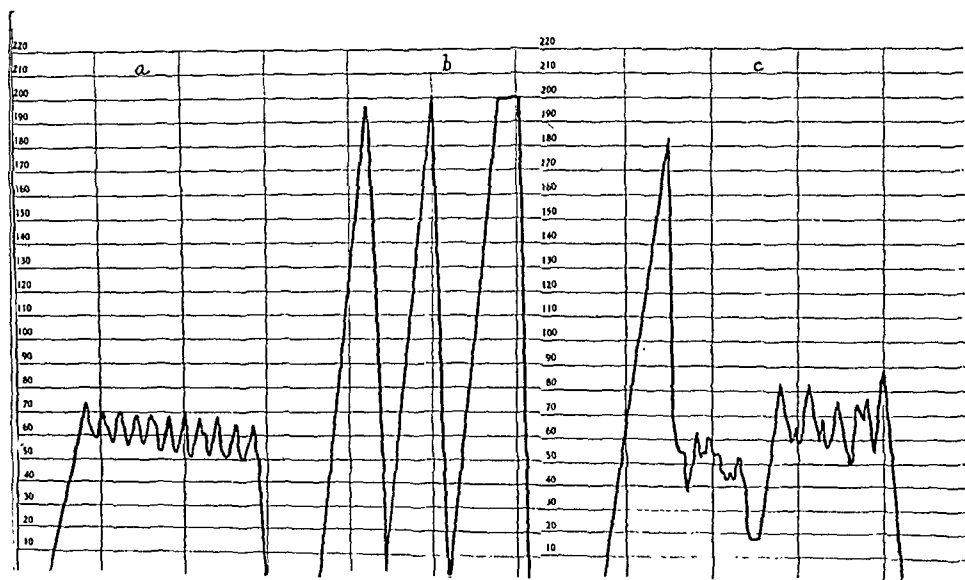


Fig. 2.—*a*, kymographic record of normal tubal patency; *b*, kymographic record of tubal nonpatency; *c*, kymographic record of uterotubal spasm.

Observations bearing upon these points were made by checking the insufflation findings by:

1. Laparotomy and clinical examination.
2. Findings after lipiodol injection.
3. Experiments upon surviving extirpated human uteri and tubes, and upon these organs removed from the sow.

#### 1. LAPAROTOMY AND CLINICAL OBSERVATIONS

Opportunity was afforded to compare the insufflation findings with observations at laparotomy in 35 cases in which tubal stenosis and peritubal adhesions were found. In 16 cases insufflation was done before and after operation; in 10 cases before operation only; and in 9 cases insufflation was done for the first time after an operation. In the latter the operative data were available and could also be judged in relation to the insufflation curves. The results were uniformly corroborative in

the 26 cases in which insufflation preceded the laparotomy. In the remaining 9 cases the insufflation findings give an idea of the present status of the tubes following operation (Figs. 3 and 4).

In the presence of peritubal adhesions without constriction of the lumen, the pressure at which the curve was maintained was not ele-



Fig. 3

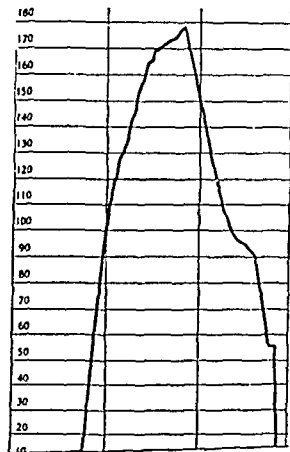


Fig. 4

Fig. 3.—Insufflation of a residual stenosed tube after a tubal pregnancy. Operative findings June 20, 1929. Rupture of a tubal pregnancy in the ampullary portion of the right tube; the left tube was found embedded in a few filmy adhesions which were separated.

Fig. 4.—Postoperative insufflation of left tube November 1, 1929, of Fig. 3. Subphrenic pneumoperitoneum right side  $1\frac{1}{4}$  inches in depth; left side one-fourth inch.

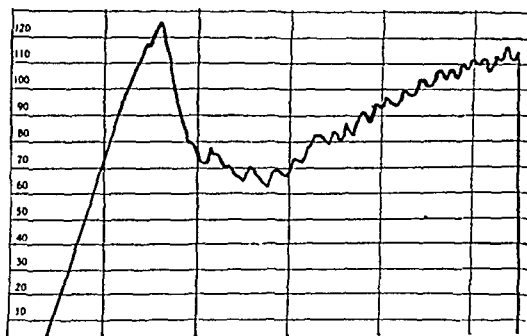


Fig. 5.—Adherent residual tube after a tubal pregnancy. Left tube was removed. The right adnexa was found adherent to the pelvic wall; adhesions were separated. Operation October 1, 1931. Graph of postoperative insufflation October 14, 1931. Positive subphrenic pneumoperitoneum; note shallow curves typical of adherent but patent tubes.

vated but the contractions were infrequent, irregular, shallow or entirely absent depending upon the degree of immobilization produced (Fig. 5).

In the presence of tubal stenosis, whether of extrinsic or intrinsic origin, the initial rise of pressure was as a rule well above 100 mm. Hg. Instead of dropping sharply and exhibiting oscillations, the curve produced was rounded and the descent gradual. When this form of curve

is produced it indicates that both tubes are mechanically impaired, because if one tube is normal the kymographic tracing assumes the normal pattern.

In judging the location of the stricture special attention was paid to the pain reaction experienced during the insufflation. Pain, as a rule, was not severe enough to cause spontaneous complaint on the part of the patient during the insufflation. On direct inquiry the patient is able to state where the pain is located and its manner of radiation.

Stricture may be located at the uterotubal junction, at the isthmus, and at points along the ampulla and fimbria. In some cases they are bilateral and symmetrical; in others asymmetrical or unilateral.

The pain location and distribution vary with the site of the obstruction.

A. *In Bilateral Strictures at the Uterotubal Junctions.*—Distention pain is present and as a rule mild, being referred to the midline in the suprasymphyseal area. There is no lateral radiation of pain.

B. *In Bilateral Strictures at the Isthmus.*—Pain is somewhat lateral, the midline pain also being present and prominent. The nearer the ampulla to the site of obstruction the more marked is the pain reaction.

C. *In Bilateral Strictures of the Ampulla.*—Pain radiates well out to the sides. The nearer to the fimbria the site of obstruction is located the greater the tendency for pain distribution; pain sometimes radiating to the lumbar region, sometimes down the thigh.

When pain is present on one side only and there are good fluctuations and a positive subphrenic pneumoperitoneum, auscultation may determine the normal tube. The bubbles in the latter instance are intermittent and correspond with the relaxation phase. If no sound is heard on the side where pain is complained of, it is presumptive evidence of an obstruction. In the presence of tubal stenosis, the gas escapes from the fimbriated end in a continuous stream which is only mildly influenced, if at all, by the very much impaired contractions of the tube. There are no silent pauses corresponding with the contraction phases of normal tubal muscle.

It is interesting to note the point at which the patient first complains of pain and when it disappears during the insufflation. Observations were made in cases with tubal closure and apply to instances of tubal strictures. In the cases with peritubal adhesions, pain occurs at a much lower level and is due to stretching of adhesions. In tubal stenosis the pain is due to distention of the proximal portion of the tube and may be maintained throughout the insufflation. As the test lasts but one or two minutes in most cases this is not intolerable. In the vast majority of cases pain was complained of when the pressure was above 110 mm. Hg and was relieved when the pressure dropped 30 mm. Hg or more.

The fluoroscopic examination is an auxiliary help. A subphrenic pneumoperitoneum was not always immediately produced in the strictured tubes where no more than 100 c.c. of gas was used because the amount of gas admitted through the narrow aperture in the tube may

not be sufficient to displace the diaphragm upwards. In exceptional instances the gas may be caught in pelvic adhesions and thus be prevented from rising beneath the diaphragm. Adhesions about the diaphragm as after an old pleurisy or subphrenic abscess may prevent diaphragmatic displacement by the gas. This is a rare occurrence. In general, it was found that when the same amount of carbon dioxide gas was insufflated the depth of the subphrenic pneumoperitoneum was shallower in the case of stenosed and adherent tubes than in normal tubes.

## 2. OBSERVATIONS FOLLOWING LIPIODOL EXAMINATIONS

Complete tubal closure has been corroborated practically in all cases by the lipiodol examination. The latter was undertaken as a further means of checking the findings and interpretations of the kymographic records in 27 cases of tubal stenosis and peritubal adhesions. A few additional cases had been examined by lipiodol and x-ray elsewhere without a preliminary tubal insufflation. The films were available and served for purposes of comparison. A striking departure between lipiodol injection and insufflation was seen as a result of this comparative study in cases of tubal strictures and peritubal adhesions. In my series only such cases which showed high grade strictures by insufflation were subjected to the oil injection.

Lipiodol has been found in this particular study to possess certain limitations that weaken its corroborative value as compared to laparotomy. For example, in two cases the lipiodol escaped from the cervix so rapidly as not to enter the tubes at all. In 8 cases the lipiodol failed to pass through either tube although insufflation had already shown adherent or stenosed but permeable tubes. Apparently, owing to its thicker consistence, lipiodol was unable to pass through the constricted lumen.

In 13 cases a diagnosis of tubal stenosis was possible from the lipiodol examinations. In 3 cases the tubes were diagnosed as patent but the degree of patency could not be determined. In only one case did the roentgenologist venture the diagnosis of adhesions by interpreting the lipiodol pictures alone. This is not surprising because peritubal adhesions, although impairing the tubal function, do not necessarily constrict the tubal lumen. Lipiodol may pass through the tubes at a relatively low pressure and appear in the peritoneal cavity shortly after its injection. Thus, no information is available as to the question of adhesions. The peristaltic wave is so infrequently demonstrated by the lipiodol plates that little dependence may be placed upon the absence of contractions with that method. It is only after noting the kymographic records obtained by uterotubal insufflation that the salpingograms become significant and then may suggest the possibility of distorted or adherent tubes.

Insufflation after the use of lipiodol in 5 cases failed to permit the passage of gas through the narrowed lumen although it passed before

lipiodol was used. In these cases the oil has a tendency to remain in the narrowed lumen as demonstrated by films which were made at varying intervals from several weeks to several years after the injection. In 2 cases an opportunity was afforded of examining the tubes histologically. Nodular tissue filled with foreign body giant cells was seen in these instances.

If lipiodol is injected without manometric control and the oil globules are seen upon the x-ray film as having entered the peritoneal cavity, nothing more is demonstrated than is shown by the crude method of uterine insufflation as first done by myself and others.

If the injection of lipiodol is not controlled by the fluoroscope and the plate is not made immediately with the cannula in place, one may not be able to say which tube is open and which tube is closed because the lipiodol is scattered in the pelvic cavity and clouds the picture of the tubes. Nor can permeable strictures be determined unless prolonged and repeated fluoroscopic examination is made and supported by x-ray films taken at stated intervals afterward. Occasionally hours and even days may be necessary before the oil shadows demonstrate that the obstruction has been passed. In spite of the numerous plates required for a diagnosis when lipiodol is used the interpretations were often difficult, taxing the skill of an expert.

Distortions of the tubes with appreciable distention will give persistent shadows with lipiodol and suggest perisalpingeal adhesions. These are lesions, however, which may be elicited by bimanual examination. The interpretation of the stenoses is more difficult when they are so tight as to allow only a small amount, i. e., a few drops of oil to escape into the peritoneal cavity. In such cases the shadows may not be distinguished from the droplets retained in the constricted portion of the tube. Even when the oil is actually seen to escape through the tube the question of stenosis is not eliminated unless manometric observations are simultaneously made. The pressure readings are not as diagnostic when oil is used as when gas is used because they are not produced by a uniformly graduated force. The uneven pressure obtained when rubber bulb or syringe is used cannot be compared to a constant flow of gas regulated by a pressure gauge.

With gas, the diagnosis of peritubal adhesions and permeable strictures may be made at once. In cases of doubt where the test has to be repeated, it is both safer and more convenient to use carbon dioxide than lipiodol.

### 3. EXPERIMENTAL OBSERVATIONS

Normal human tubes as well as the oviducts of the sow which have been removed from the body can be made to survive when immersed in Locke's solution through which oxygen is insufflated. The oxygen may be allowed to pass through the tube lumen as in clinical uterotubal insufflation. Under these conditions the tubes have been shown to exhibit

rhythmic contractions quite identical with those obtained when the tubes are insufflated in vivo.

When the cannula carrying the oxygen is inserted into the fimbriated end of the tube the contractions may be recorded on the kymograph. Records similar to those obtained by the clinical application of the test may be duplicated when the cannula is fitted into the cervix of the specimen of the uterus and tubes.

If the tubes are adherent to the uterus or the ovaries or the intestines the tracings obtained show a striking alteration (Figs. 6 to 13). It

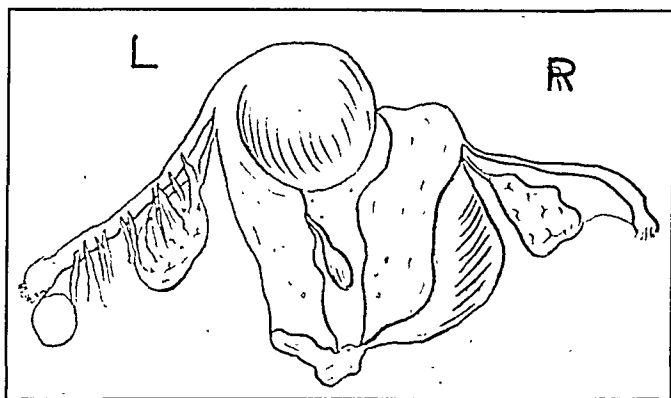


Fig. 6.—Sketch of a specimen showing fundal submucous fibroid and polyp. Peritubal adhesions surround left tube.

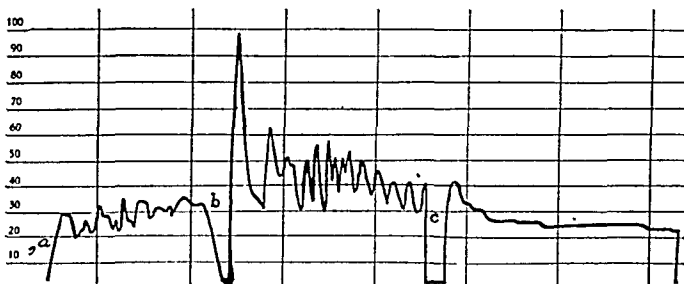


Fig. 7.—*a*, Graph of both tubes; (Fig. 6) *b*, graph of right tube, left tube being held shut between fingers; *c*, graph of left tube (peritubal adhesions) when right tube was held shut between fingers. Experiments shown in Figs. 9 to 15 were made upon this specimen.

should be mentioned that the material used for this purpose must be removed with care so that conditions found at laparotomy are preserved. Special care was therefore taken not to disturb the natural relations of the organs removed. When the kymographic records produced by insufflating the specimens were compared with those obtained by clinical uterotubal insufflations, it was found that the resemblance was most marked.

As the surviving tubes reproduce contractions similar to those obtained in the intact state they offer an opportunity to note what effect mechanical simulation of adhesions and strictures might produce. Accordingly, normal fallopian tubes were insufflated and records obtained

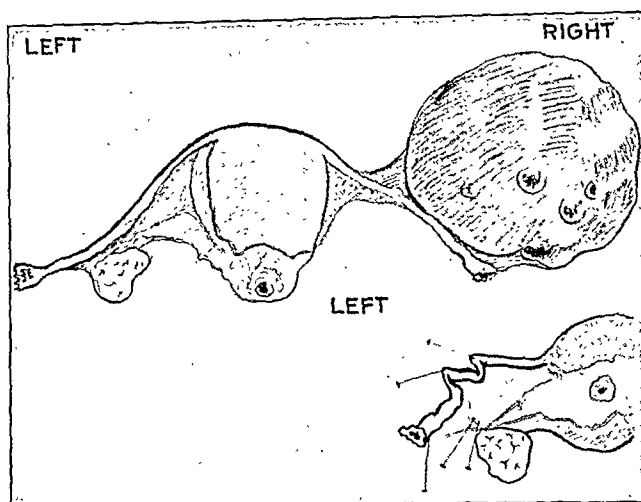


Fig. 8.—Sketch of specimen showing left tube normal in contour and patency. The right tube is adherent along its entire length to the dermoid cyst of the right ovary (size of an orange).

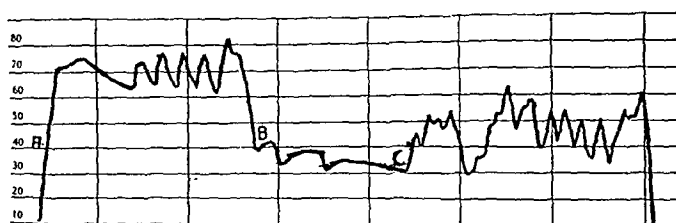


Fig. 9.—A, Graph of left tube while right tube is being compressed at uterine end. B, Graph of right tube; left tube compressed at uterine end. C, Graph of both tubes; compression released.

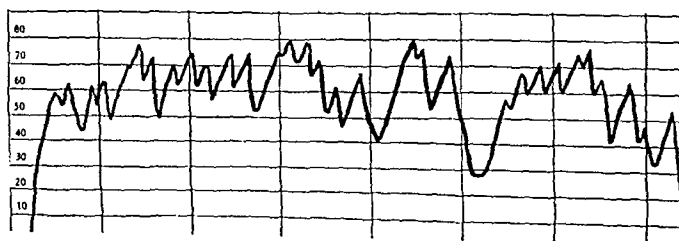


Fig. 10.—Graph of left tube; right tube compressed at uterine end.

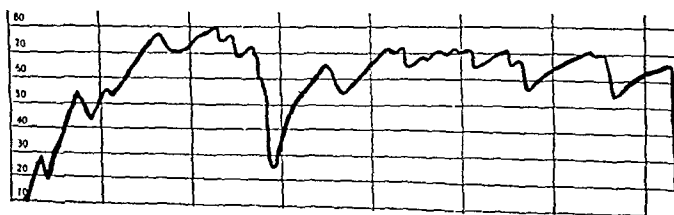


Fig. 11.—Graph of right tube; left tube compressed at uterine end.



for comparison. Peritubal adhesions and tubal stenosis were then artificially produced by: (1) immobilizing the tubes with pins; (2) constricting the tubes with weights; (3) constricting the tubes with clamps; (4) constricting the isthmus alone after the ampulla was excised; and (5) twisting the uterus so as to constrict the tubes.

1. *Effect of Immobilizing the Tubes With Pins.*—The tubes were placed upon a cork plate and were transfixated by fastening pins through the serosa at several points (Fig. 14).

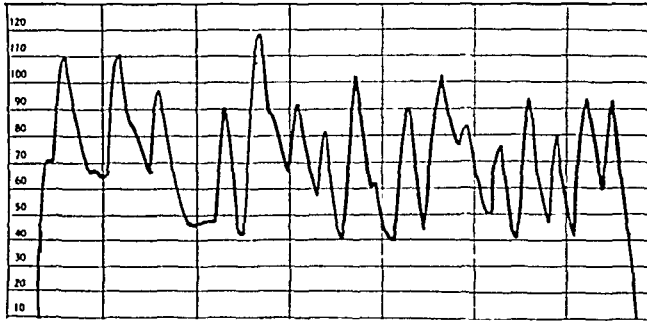


Fig. 12.—Graph of both tubes; marked contractions after the tubes had been irritated by heat and pinching.

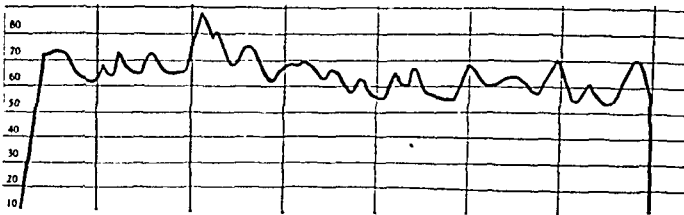


Fig. 13.—Graph of right tube; left tube transfixated by pins as in diagram.

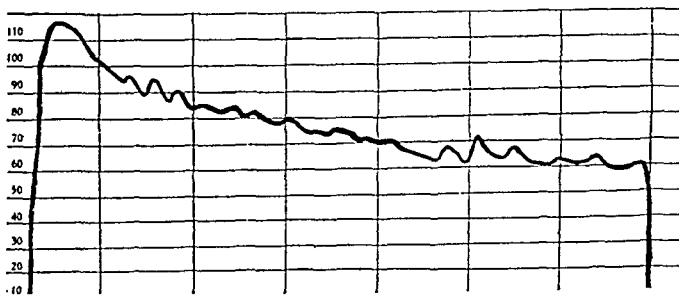


Fig. 14.—Graph of transfixated left tube; right tube is compressed at uterine end.

If the tubes are transfixated by pins without causing distortion or angulation, the initial rise in pressure may not exceed 100 mm. Hg but no well marked fluctuations are seen. The tubes do not undergo peristaltic or pendulum motion and the waves of contraction are inhibited. This is graphically represented on the kymograph.

If only one side of the tube is transfixated, i. e., along the mesosalpinx leaving the opposite surface free, the tube exhibits normal contractions and the initial rise of pressure is not unduly high. The gas in the latter instance flows out of the tube in intermittent bubbles instead of in a constant stream which is observed when the tubes are held down by adhesions or are the seat of well marked strictures.

If the isthmus alone is pinned down and the remaining tube is left in its normal condition, only a rare contraction, if any, occurs. If part of the isthmus is left free, irregular and infrequent contractions occur. With the isthmus free and the ampulla pinned down the type of tubal contractions is but little affected; a slight irregularity in rhythm may be noted.

When the pins are removed if the experiment is not delayed too long after removal of the organs and while they are still in a good state of preservation, they may regain their former contractility and describe curves in a rhythmic fashion.

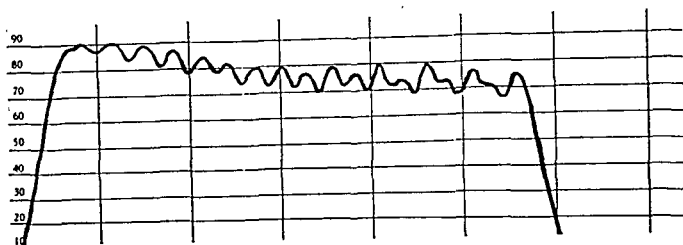


Fig. 15.—Graph of right tube; left tube is compressed at uterine end.

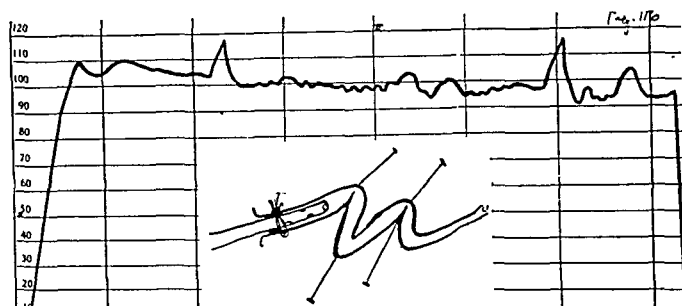


Fig. 16.—Showing graph of experimental duplication of peritubal adhesions, showing cannula in the fimbriated end of human tube, and graph of tube transfixed by pins as in diagram.

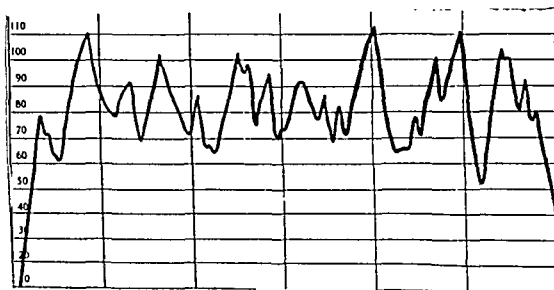


Fig. 17.—Graph of tube after the pins were removed one hour and fifteen minutes from the beginning of the experiment.

2. *Effect of Constricting the Tubes With Weights.*—The artificial duplication of an internal stricture is more difficult to produce than external constriction. The latter may be actually produced by applying weights or clamps to the tubes.

Applying weights to the tubes was found to produce an elevation of the pressure at which contractions were maintained and an irregularity in the rhythm and depth of the contractions directly proportional to the amount of constriction produced. When the lumen was but slightly obstructed, the initial pressure rose to about 100 mm. Hg; the contractions became infrequent and irregular but maintained a fluctuation range even as high as 40 mm. Hg. With increased weight the constriction could be augmented to the point of complete tubal closure.

3. *Effect of Constricting the Tube With Clamps.*—Constriction of the tube was reproduced by applying clamps of the Murphy regulating type at different points along its length. The character of the kymographic curve resembles in appearance that of a clinical pathologic stenosis of the tubes (Fig. 15).

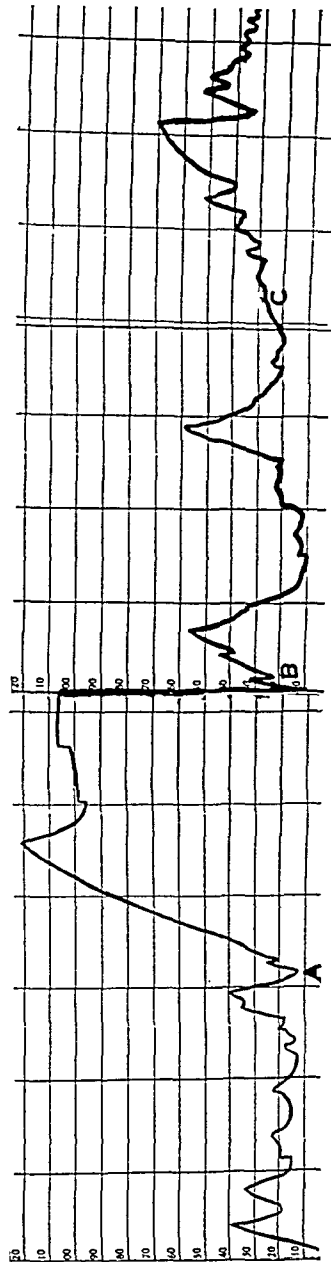


Fig. 18.—Experimental duplication of tubal stenosis and adhesions; uterotubal insufflation of pig's tube at interestrus. A, Isthmus compressed by clamp without complete closure. B, Isthmus transfixed without distortion as in diagram. C, Ampulla then transfixed as in the diagram (Fig. 19). (Pins removed from isthmus.)

It has been found in the course of experiments that there is a decided difference between isthmic and ampullary strictures. This depends upon the specifically different type of contractions each of these segments possesses under normal conditions.

In the case of human tubes, the intramural portion and isthmus appear to exhibit the most marked contractions. These may be observed when insufflation is directed toward the abdominal end or the uterine end of the tubes and parts of the tube are progressively excised. If the isthmus is removed leaving the ampulla in-

tact (fimbriated insufflation) the contractions are shallower and may even be absent.

In one clinical uterotubal insufflation I had the opportunity of noting the type of curves produced when only one ampullary fimbriated portion was present. This portion had been implanted into the uterine horn, the isthmus having been excised



Fig. 19

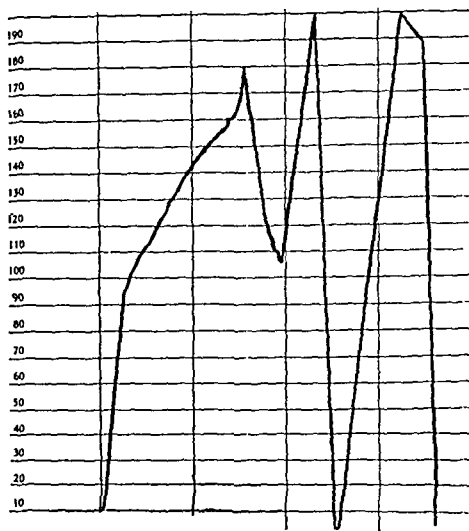


Fig. 20.

Fig. 19.—Pig's oviduct and uterine horn transfixed at the isthmus and ampulla.

Fig. 20.—Graph of the ampulla after a tubouterine implantation. Insufflation before operation July 19, 1930. Nonpatency.

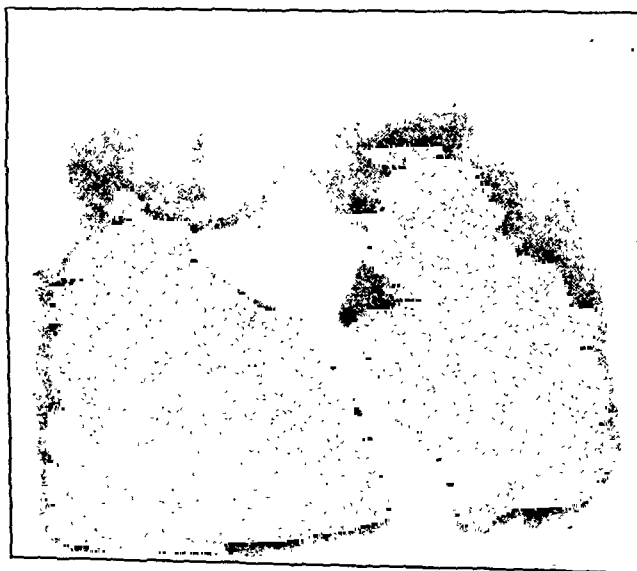


Fig. 21.—Lipiodol examination before operation August 23, 1930; showed both tubes to be completely blocked at the uterine end. Same case as Fig. 20.

and the other tube removed for advanced nodular salpingitis. No contractions occurred and the pressure maintained was not unduly high (Fig. 16).

Contractions are exhibited by the tube whether the insufflation is directed toward the abdominal or the uterine end. In the pig the frequency of the tubal contractions varies, however, with the estrus interval. Thus the contractions obtained by utero-

tubal insufflation at estrus are regular and occur at a rate of about 15 to the minute, whereas only irregular, less frequent contractions occur when fimbriated insufflation is performed. The reverse holds for the interestrus interval.\* These results have not been studied systematically in the human tubes.

Experiments were carried out on intact tubes in which the isthmus and ampulla were clamped separately, and upon the isthmus alone after the ampulla was removed. Constricting either the isthmus or ampulla resulted in an elevation of the pressure which was sustained as long as the gas flowed through the tubes. Contractions were

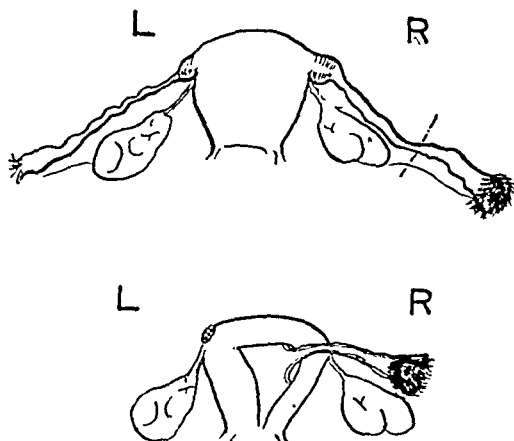


Fig. 22.—Operation October 7, 1930. Both tubes were found obliterated by nodules at their uterine end. The left tube was removed. The nodular portion of the right tube was resected and the ampulla with the fimbriated end, tested for patency by syringe and medicine dropper, were implanted into the fundus. Same as Fig. 20.



Fig. 23.—Insufflation after operation November 24, 1930; showed the implanted ampullary portion of the right tube to be patent at a pressure of 145 mm. Hg but there were no contractions. A second insufflation done immediately afterwards gave a pressure of 98 mm. Hg with similar type of curve. Same as Fig. 20.

absent for the most part or at times infrequent and irregular depending upon the degree of stricture produced. The paralyzing effect upon the contractions was more marked when the isthmus was clamped than when the ampulla was constricted. The same result was obtained when the isthmic stump was clamped after the ampulla had been excised.

4. *Effect of Constricting the Tubes by Twisting the Uterus.*—In order to note the effect produced by torsion of the tubes upon both pressure and contractions, the

\*The experiments dealing with this subject were made in Prof. Corner's laboratory and will be published by Mr. Maurice Whitelaw, medical student at Rochester Medical School.

uterus with the tubes attached was twisted upon itself. When the uterus was twisted to 180 degrees, there was little effect noted. When it was twisted to 270 degrees the pressure at which contractions were maintained was about 20 mm. Hg higher; contractions, however, continuing as before. As the amount of torsion was increased the contractions became less frequent and more shallow until, when the uterus was twisted to 360 degrees, closure resulted and the pressure exceeded 200 mm. Hg.

#### SUMMARY

1. The diagnosis of nonpalpable tubal adhesions and tubal stenosis can be made by uterotubal insufflation with the aid of the kymograph. It is based upon the fact that tubal contractions in the presence of these lesions are completely absent or markedly changed. Observations were made at laparotomy where these lesions were found affording an opportunity of checking the insufflation findings. Characteristic curves were produced.

2. In the presence of tubal stenosis, whether of extrinsic or intrinsic origin, the initial rise of pressure was as a rule well above 100 mm. Hg. Instead of dropping sharply and exhibiting oscillations the curve produced was rounded and the descent gradual. Fluctuations were absent as a rule.

3. In the presence of peritubal adhesions without constriction of the lumen, the pressure was less elevated. The contractions were infrequent, irregular or shallow and at times entirely absent, depending upon the degree of immobilization produced.

4. The location of pain elicited during the performance of the test as well as the auscultation findings were found to vary with the site of obstruction.

5. Roentgenologic examination of the tubes after lipiodol injection proved of less value than laparotomy in checking the insufflation findings of peritubal adhesions and tubal stenosis. The disadvantages of the oil in this respect were due to: (1) its rapid escape from the cervix in some cases; (2) its inability to pass high grade strictures in most cases, and (3) its tendency in the strictured tubes to produce foreign body reactions.

6. Insufflation of the excised but surviving uterus and tubes reproduce curves similar to those found by clinical uterotubal insufflation where adhesions and strictures were present. By artificially reproducing immobilizations and stenosis of the tubes, the paralyzing effect upon rhythmic tubal contractions and tubal peristalsis was also demonstrated.

# THE INFLUENCE OF AGE AND RACE ON THE DURATION OF LABOR

C. H. PECKHAM, M.D., BALTIMORE, MD.

*(From the Department of Obstetrics, the Johns Hopkins Hospital and University)*

IT HAS long been felt that from a strictly physical point of view, the young woman of fifteen to twenty years of age makes the most satisfactory obstetric patient, and that a definite correlation exists between increasing age and various abnormalities and accidents of pregnancy, labor, and the puerperium. In recent communications the author has drawn attention to the fact that with increasing age the maternal and fetal mortality, as well as the incidence of operative deliveries, becomes considerably greater. The purpose of this study is to investigate the influence of age on the duration of labor, and particularly to ascertain whether any differences in this respect exist between the white and black races, as the two about equally make up the population of this clinic.

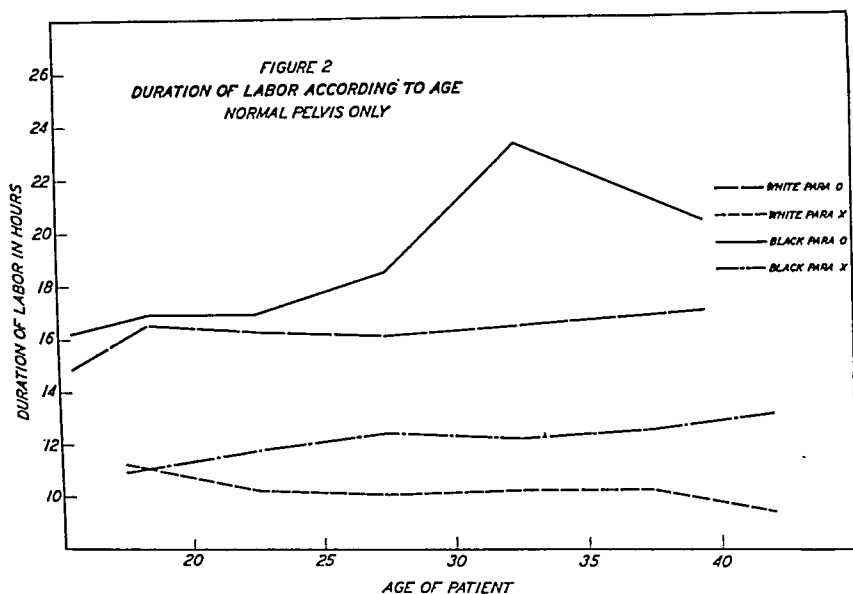
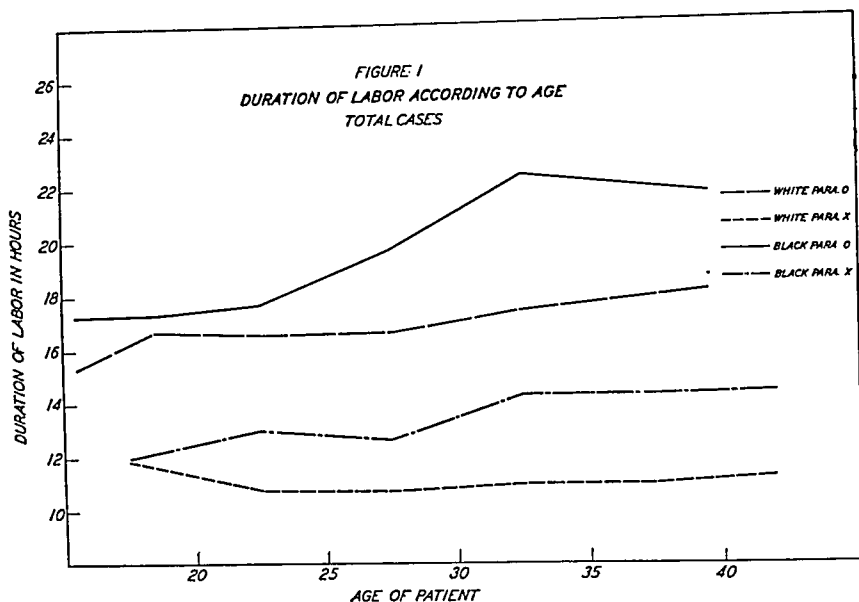
For this purpose we have used the same material as in the above mentioned articles; namely, a series of 15,370 consecutive deliveries, premature and fullterm, occurring in the Johns Hopkins Hospital during the period from January 1, 1907, to December 13, 1929. Except for computing the mean duration of labor the patients delivering prematurely have been discarded, as well as those delivered by cesarean section, and a few in whom the case records were lacking in definite information as to the duration of labor or the age of the patient. There remains a total of 13,658 patients, delivered at or near term through the birth canal, and divided by color and parity into the groups shown below.

	WHITE	BLACK	TOTAL
Primiparae	3742	3880	7622
Multiparae	3352	2684	6036
Total	7094	6564	13,658

An analysis was first made of the total cases in the series. The mean duration of labor in both primiparae and multiparae is longer in the black than in the white women. Thus the average primiparous labor in the white lasts 16.57 hours as contrasted with 17.66 hours in the black race, while figures of 10.91 and 12.49 hours obtain for the two groups among the multiparae.

The difference between the two races and the effect of increasing age is graphically illustrated in Fig. 1. From this it will be seen that in the white race the duration of labor tends to increase, although not strikingly, in the older age groups, both primiparae and multiparae. Thus, while the mean duration in white primiparae remains approximately 16.7 hours from the age of seventeen to thirty, it rises thereafter and in

women above the age of thirty-five reaches 18.05 hours. A similar, though less marked tendency is observed among the multiparae. Among the black women the rise in the later age groups is much more significant. Thus, in the group of black primiparae aged twenty to twenty-four, the mean duration of labor is 17.67 hours, but rises thereafter so that



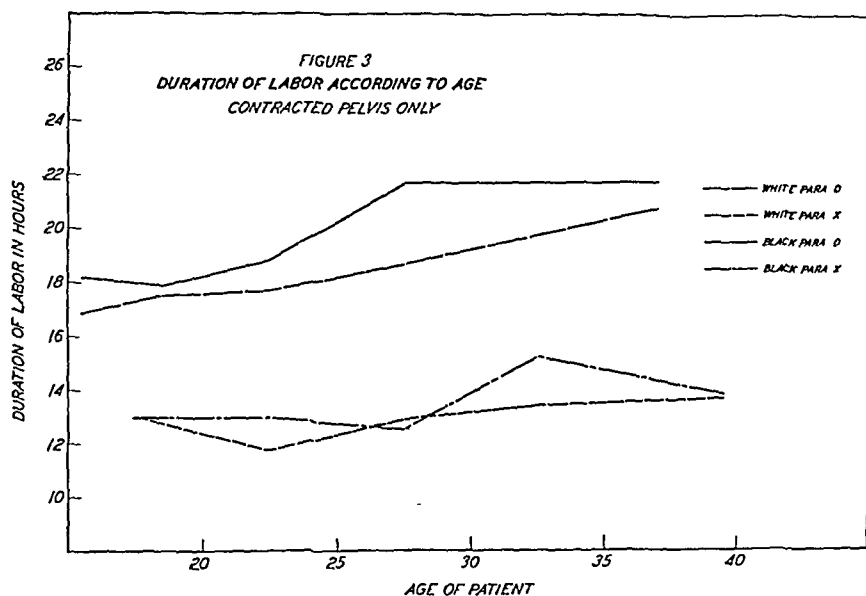
above the age of thirty-five years a figure of 21.67 is reached. A similar trend though again less marked, was found among the multiparae of this group.

Fig. 1 then, indicates an apparently significant racial difference in the duration of labor. In searching for an explanation of this rather



unexpected finding, it at first seemed probable that the higher incidence of contracted pelvis among the blacks might play a rôle in causing prolongation of their labors, since some degree of pelvic abnormality is observed in 45 per cent of the black as contrasted with less than 20 per cent of the white women in the clinic population.

Accordingly, a similar analysis was made of the material at hand omitting all cases of contracted pelvis, and excluding outlet as well as inlet contractions. The results of this study are illustrated in Fig. 2. Again, in the black primiparae, the mean duration of labor is significantly prolonged over that of the white, particularly in the older age groups (above thirty years), while in the multiparae there is at least a two hour difference from the age of twenty-five on.



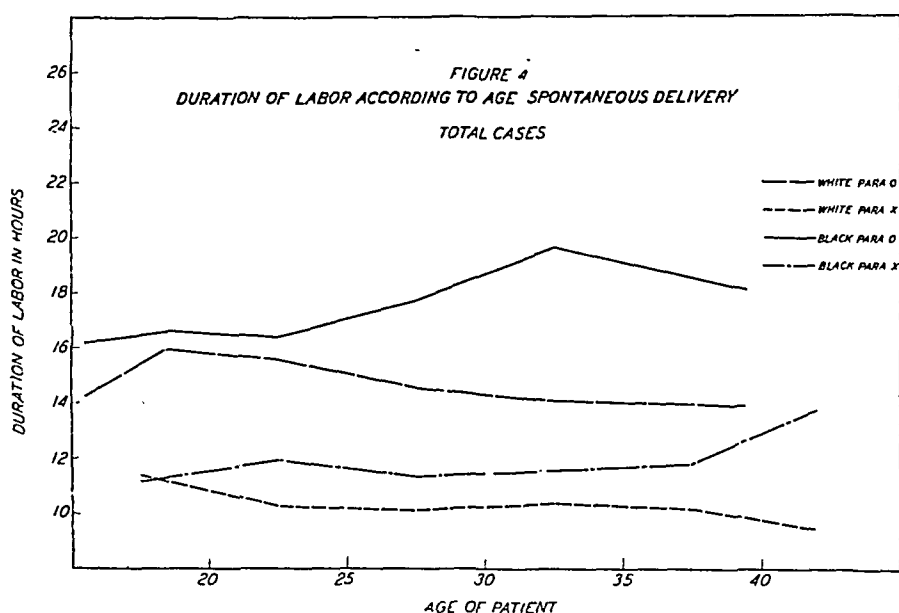
It will also be noted from Fig. 2 that in the white patients, both primiparae and multiparae, there is almost no increase in the duration of labor in the older age groups, the figure of seventeen hours for the elderly primiparae (above thirty-five) being only nine-tenths hours above that of the age group twenty-five to twenty-nine, the low point for this group of cases above the age of sixteen. However, in the black women there is a notable tendency toward longer labors in the higher age groups, which is more pronounced among the primiparae than the multiparae. •

Fig. 3 indicates that in the group of patients with contracted pelvises the racial differences are less marked. However, the colored primipara still has a longer labor than the white, whereas the difference between the multiparae of the two races is probably too small to be significant. Both races here show a tendency toward longer labor with increasing age. Indeed, the primiparae aged thirty-five and over in both races have a

mean labor lasting about three hours longer than in the age group twenty to twenty-four.

It may be stated that the entire series of cases regardless of type of pelvis, indicates that those labors terminated by some operative procedure are constantly several hours longer than in the group of spontaneous deliveries. This is true of the multiparae as well as primiparae, and is not surprising. However, it seems noteworthy that in the black race the difference in the length of labor in operative over spontaneous deliveries is constantly greater than that observed among the whites.

In our effort to arrive at the true differences in the duration of labor according to age and race, it next seemed advisable to omit as a complicating factor all operative deliveries. Fig. 4 presents the average labors

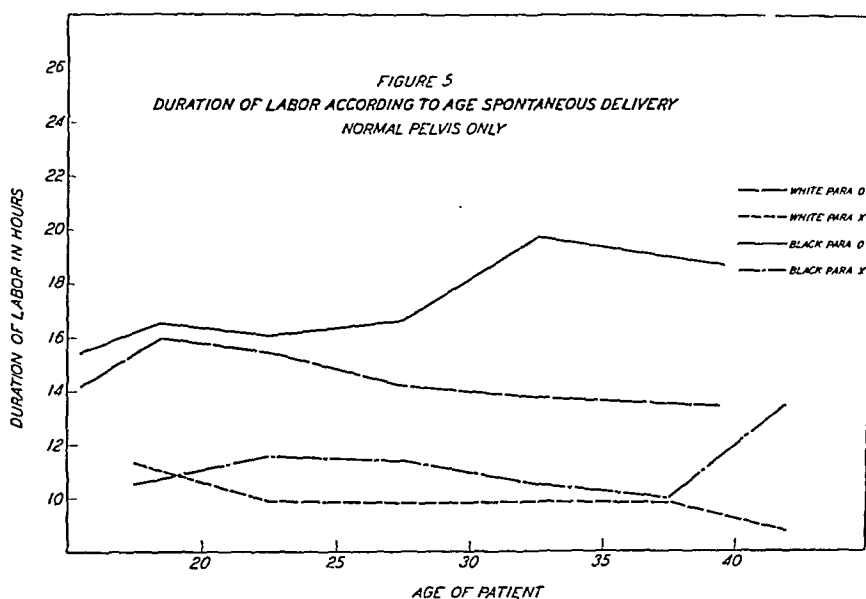


in the different age groups terminating without any operative interference. The racial differences hitherto observed are still found to persist, and indeed among the primiparae over twenty-five years of age are greater than when the operative groups were included. No increase in the duration of labor with age is observed among the white women and in fact there is a steady trend downward in the older age groups, as it is found that the mean duration in primiparae over thirty-five is 2.06 hours less than those aged seventeen to nineteen, the group with the longest mean labor for this type. Among the black women, however, the duration of spontaneous labor is still increased in the older age groups, and more noticeably so in primiparae than multiparae.

Fig. 5 would appear to indicate most accurately the real effect of race and age on the duration of labor, for here only those cases terminating spontaneously and with normal pelvises are considered. The mean duration of labor among the black multiparae is 11.20 hours, a figure 1.28

hours above that obtaining in the white, and with multiparity no tendency is noted toward the prolongation of labor by increased age in either race, indeed, in the black women above the age of forty a definite increase has taken place. The number of cases on which this figure is based are, however, so small, as to make one suspect that it may be due to a sampling error. The case for the primiparae is, however, quite different. The labors in the black women are longer throughout, and significantly so after the age of twenty-five. In the higher age groups the mean duration falls in the white and rises in the black patients, so that after the age of thirty-five is reached the difference becomes 5.31 hours.

The average length of labor, based on a large series of cases at or near



term, but excluding cesarean section, is approximately seventeen hours and forty minutes in black primiparae, as contrasted with sixteen hours and thirty-four minutes in the white, whereas in the multiparae we find figures of twelve hours and twenty-nine minutes and ten hours and fifty-five minutes for the two races, respectively.

The length of labor is relatively little affected by degrees of pelvic contraction which permit delivery through the birth canal. Thus, in white primiparae with normal pelvises the mean duration is 16.25 hours, as contrasted with 17.91 hours where some degree of contracted pelvis exists, while in black primiparae figures of 17.03 and 18.49 hours obtain. Similar differences are found in the multiparae of the two races.

#### DISCUSSION

An analysis of the effect of race and age on the duration of labor in a series of 13,658 consecutive deliveries at or near term reveals a sur-

prisingly constant difference between white and black women. Regardless of age or parity, the black patient has a longer labor than the white. The difference is not particularly marked in women under twenty-five years, but after this age it increases to several hours. The explanation for this phenomenon is not clear. It seems evident, however, that it is not due to the higher incidence of contracted pelvis among the blacks, for a study of the patients with normal pelvises shows the same disparity as when only those with contracted pelvises are considered. This racial difference becomes even more difficult to explain when one recalls the increased malleability of the fetal head and the smaller weight of the infants in the black race. Thus, in a series of 2,000 deliveries at or near term, and equally divided between the two races, the mean weight of the black and white infants was 3155.9 gm. and 3379.9 gm., respectively, a difference of 224 gm. or 7½ ounces. The patients in this series, however, represent mostly the dwellers in the tenement districts of a large city, and it seems likely that such an environment has produced degenerative changes in the black race, which is increasingly incapable of easy childbearing.

Our figures show that in both races there is a tendency for the duration of labor to increase with advancing age, a phenomenon much more marked in the black than in the white women. Thus, a consideration of the total patients in the series reveals an average labor of 15.30 hours in white primiparae under the age of sixteen which rises to 18.04 hours in women thirty-five years or older, whereas in the blacks of corresponding age, figures of 17.24 hours and 21.67 hours respectively obtain. The same tendency, although not so marked, obtains in the multiparae of each group. On the other hand, when our consideration is limited to women with normal pelvises, almost no rise in mean duration is noted among the whites, although labor is definitely prolonged in the older age groups in the black race.

A consideration of the cases in the series delivering spontaneously, including both normal and contracted pelvis, shows a decrease in the mean duration of labor among white women, both primiparae and multiparae. Thus in white primiparae aged seventeen to nineteen, the average labor lasts 15.97 hours, while in similar patients aged thirty-five or over, it is only 13.91 hours. On the other hand, a rise in mean duration still occurs in the blacks of older age as is evidenced by figures of 16.20 hours and 18.13 hours in primiparae below seventeen and above thirty-four years, respectively.

Finally, when only those patients with normal pelvises who deliver spontaneously are included, we again find a definite drop in the duration of labor among whites of the higher age groups, although among black primiparae of similar age an increased duration of labor is still noted.

This study indicates that in still another way, i. e., length of labor, the black woman is a less satisfactory obstetric risk than the white. Since in

an accompanying article we will demonstrate that fetal mortality increases directly with the duration of labor, it seems probable that the increased duration among black women accounts to some extent for the higher fetal mortality in that race.

Contrary to the general belief, our figures show that there is very little increase in the duration of labor with advancing age among white women. Indeed, in those delivering spontaneously a decrease in mean duration is observed in the older age groups. Including all cases, spontaneous and operative, normal and contracted pelvis, the mean duration of labor in primiparae aged thirty-five or over is only 1.38 hours greater than that recorded for those between seventeen to nineteen years of age, while for multiparae even less increase is seen with age. Consequently, it seems probable that the increased operative incidence and higher fetal mortality observed in the obstetrically elderly woman is chiefly to be explained in terms of rigid soft parts affecting the second stage of labor, and that the first stage progresses as normally and approximately as rapidly as in the younger woman. This reasoning, however, does not apply to the black race where definitely prolonged labors are observed with increasing age.

#### CONCLUSIONS

1. An analysis has been made of the effect of age and race on the duration of labor in a series of 13,658 consecutive deliveries at or near term.

2. Black women, both primiparae and multiparae, and regardless of age, have consistently longer labors than white.

3. In both races, a consideration of total cases reveals an increased duration of labor in the older age groups, which however is more marked among black than white women.

4. Omitting cases of contracted pelvis, this age increase persists in the black but almost disappears in the white race.

5. Considering only those cases delivering spontaneously, the duration of labor tends to fall with advancing age in white patients, even primigravidae, although it increases in black women regardless of parity.

NOTE: A series of tables giving in detail the statistical data on which this paper is based has been omitted owing to lack of space.—*Editor*.

# CLASSIFICATION AND TREATMENT OF DYSPAREUNIA\*

MAX D. MAYER, M.D., NEW YORK

*(From the Gynecological Service of the Mount Sinai Hospital)*

THE arrangement on the Gynecological Service whereby each morning clinic of the Out-Patient Department is reserved for the study of a special group of cases, has made it possible to concentrate the series of cases of dyspareunia.

The treatment of dyspareunia must be individualized because the cases do not conform to a single type. They vary as to cause, as to the individuals, and as to the domestic situation.

In general, the causes may be classified as follows:

## 1.—Organic:

(A) Introital: rigid hymen; reflex spasm from trauma or infection or both; operative overcorrection of plasties; atrophy of the senile type and that following x-ray treatment; kraurosis; urethral, e. g., caruncle, urethritis, cystitis; anal fissure; neuritis of the pudic nerve.

(B) Pelvic: diseased adnexa; shortened parametria; prolapsed ovary.

## 2.—Psychogenic:

(A) Initial dyspareunia: fear of injury (narcissistic type); fear of pregnancy; as a symptom of severe neurosis; as a symptom of psychosis.

(B) Secondarily acquired dyspareunia: fear of pregnancy; hysterical manifestation (of a negative attitude toward the husband, equivalent in many cases of frigidity).

## 3.—Combinations of Organic and Psychogenic:

The above may be combined in any quantitative relationship: (a) Where an organic lesion is secondarily invested with a mental significance, with emphasis on the factor of morbid gain. (b) Where a vaginal spasm has led to secondary organic changes, as for instance, the results of trauma from attempts to overcome it.

## DIAGNOSIS

First importance should be given to the history; not only the material, but the way of eliciting it. It should go without saying that the first step is to estimate the personality of the patient and make every effort to get a certain measure of confidence before proceeding with the history itself. In addition to the ordinary gynecologic history, it is essential to determine the familial setting, the developmental history, other complaints, and other experiences in the past. Among the most important of the facts in the present history are the severity, duration, onset, the patient's attitude toward the complaint and to her mate, the previous attempts at treatment, the frequency, duration, position, etc., of coitus, the presence or absence of orgasm. One should realize the transference situation in taking the history, and that often there is an initial attitude toward the doctor as an enemy who threatens to duplicate a painful situation and who somehow seems to be in alliance with the husband, against whom the symptom may be a defense.

\*Read at a meeting of the Section on Obstetrics and Gynecology, New York Academy of Medicine, January 19, 1932.

## TREATMENT

This will, of course, depend upon the type of dyspareunia and its cause. It may be classified as follows:

1. Prophylactic: May I mention at this point that Dr. Dickinson in his articles and numerous discussions on the subject of premarital instruction as well as in his excellent study of *A Thousand Marriages*, has correctly emphasized the importance of prophylaxis, and I can do no better than to refer you to his recommendations. Unfortunately, the gynecologist, both in clinic and office practice, sees the majority of cases when it is far too late for prophylaxis.

2. Actual Treatment: The actual treatment should be radical. If the cause is mental, the treatment should be mental, though it must be understood that this does not preclude local measures and that the patient may very well attribute a cure to these local measures. The treatment of the husband in these cases may be of great and even paramount importance. Incidentally, there is a high incidence of gentle, timid and inexperienced men, often relatively impotent, among the husbands of these women with primary dyspareunia. Perhaps this is due, in part, to their unconscious selection, on the somewhat mistaken assumption, that a gentle person would hurt them less; in part, it is the result of far more complex, deep-seated, psychologic reasons that I cannot enter into now, except to state that they are associated with their castration anxiety and envy of the male.

A. Rigid Hymen: The hymen will have to be stretched or cut. It might often seem simpler to cut it, yet actually, it is more practicable to stretch it by gradual dilatation. In cases of local trauma, vulvitis or vulvovaginitis, the inflammation must be treated before any attempts at stretching are made. One cannot over-emphasize the need for the most scrupulous care to avoid the slightest pain. Douching is in most cases inadvisable. A useful method is to insert an endoscope, and through this, a strip of gauze impregnated with Lasar's paste. This keeps the surfaces apart and dry and has the additional advantage of preventing any attempts at coitus. It should be changed daily.

B. Postoperative. Postoperative dyspareunia is the result of various types of operative misjudgments. (1) Too high a perineum of the shallow type may act as a thin commissural band which has the effect of a hymen. (2) Too narrow a vagina as the result of sacrificing too much mucosa in the anterior plastic. (3) Too tight levator sutures catching the muscle bundles with the consequent constriction ring at the vagina. (4) Too tight a vagina left after a vaginal hysterectomy. The treatment will depend upon the severity of the case. Some cases respond to non-operative dilatation which should be tried. Others require the so-called reverse plastic in which a nice judgment must be exercised to maintain the proper balance between the coital and supportive functions.

C. Atrophy: In the senile type of atrophy the relative infrequency of coitus plays a rôle and it seems important to prevent further shrinking by the wearing of vaginal plugs of appropriate size for rather considerable periods at regular intervals. Good lubrication is very important, and in douching one should avoid the stronger astringents. The hormonal treatment of these cases is feasible, but at present not practicable.

D. In the urethral type of dyspareunia, it seems advisable to toughen the meatus

with proper applications, but more important is instruction in altering the coital position to avoid catching the urethra underneath the pubic arch. "A posteriori" sometimes answers the purpose very well.

E. In the case of dyspareunia due to diseased adnexa. In addition to the usual general, hydrotherapeutic and thermal method, the *colpeuryxis* treatment with mercury is sometimes very efficacious. If because of the great chronicity of the condition, coitus cannot be interdicted, the following position should be advised: After intromission in the lithotomy position, the woman's thighs are fully extended and approximated, her knees inside the slightly separated knees of the man. This gives the minimum penetration, the minimum pelvic pain without sacrificing mutual stimulation.

F. In the cases of prolapsed ovary, the insertion of a Hodge pessary worked very well in two cases.

G. In the cases of dyspareunia associated with shortened parametria, the treatment is more or less like that with diseased adnexa.

### PSYCHOGENIC

The treatment of psychogenic dyspareunia commands extended attention. Obviously, one cannot enter here into the intricacies of the dynamics of its genesis. In the severer cases, this is a task for the specialist. It is very important for the gynecologist to recognize and differentiate those cases in which he can reasonably expect to get a good result from the suggestive measures at his disposal and those which he had better refer to a psychotherapist.

This much should be said: that the majority of cases of dyspareunia coming to the gynecologist are primarily psychogenic, although all the cases have some psychologic factors. The more these factors are taken into account, the more efficacious the treatment. It is of great importance to interview the husband, as obviously he may be the one to require attention.

In approaching the treatment of psychogenic dyspareunia, it seems advisable for the time being, to forget anatomic considerations and consider the individual. The cases may be simply grouped into:

1. The mild, in which there is a somewhat excessive reaction to an unfavorable situation, as for instance, an inept, inexperienced husband, an unusually thick hymen, a timid individual; the patient is cooperative and has insight. In these cases, the treatment can be rapid and one can very well combine local treatment with psychotherapy in the following way:

This method embodies the dynamics of the psychotherapeutic cure without any attempt to give the patient conscious insight. In this respect it is similar to many forms commonly used in medical treatment, but differs in that the physician is more or less aware of the mechanism.

At the first visit the patient is interviewed, (mostly listened to) and preferably not examined. When an examination is made, it is but an inspection. There should be no pain. The doctor concentrates his efforts in gaining the woman's confidence.

An endoscope is inserted through which a wick of medicated gauze is passed and left in. At subsequent visits very gradual and mechanical dilatation, combined with the local treatment, finally permits the easy introduction of a small vaginal speculum. This is replaced by a series of graduated test tubes, up to  $1\frac{1}{4}$  in. in diameter. Then the patient is shown how to introduce this test tube herself, which she does with ease. Then she is given the test tube and instructed to introduce



it herself at home for several days. The husband is then interviewed and instructed, and all treatment tentatively discontinued before the couple make any attempts at coitus.

The underlying principle is the establishment of confidence and the transference through which the fear, resentment and anxiety are partially overcome. This permits the alleviation of the local condition by a mechanical means which is presently replaced by an instrument with phallic significance. The patient is encouraged to be cooperative in its introduction. The treatment is then terminated and the patient returns to her coital function with an altered point of view. I do not think one need fear the danger of instituting autoerotism, principally because these women are not yet vaginally erotised.

2. The severe. In severer cases we see an inadequate response to a not unusual situation; there is no disproportion; there are other manifestations of a neurotic make-up; cooperation is not complete and insight is often lacking. In these cases, the treatment should be psychotherapeutic purely, up to the point where the patient is herself desirous of instituting local treatment.

3. The extremely severe forms, as for instance, in the cases of persistent virgins for many years; we must be extremely cautious. They are frequently psychopathic personalities. Interference here is not without considerable danger of a complete breakdown and even suicide.

#### ACQUIRED DYSPAREUNIA

In the first group resulting from fear of pregnancy, one may combine a brief psychotherapy with adequate contraceptive advice. In the group in which the dyspareunia is a result of a negative reaction against the husband, local treatment is of no avail. Brief psychotherapy of the suggestive type is almost always doomed to failure. Prolonged psychotherapy only offers a reasonably fair prognosis as far as the dyspareunia is concerned; though the prognosis is poor, quoad frigidity.

Combinations are treated after a careful evaluation of the factors. I do not wish to convey the impression that the rapid treatment, or for that matter, any treatment offers a guarantee for cure. Many cases do not respond rapidly. One cannot emphasize too strongly the necessity for individualization of the cases as well as the necessity for the utmost patience.

Dyspareunia, then, is due to a variety of causes, that manifests itself in all degrees of severity. The causes may be organic or mental or combinations of both. Treatment should be instituted in both directions. The condition may seem a minor one, when it is really of major importance in the life of the individual. There is a need for marked individualization of the cases. The prognosis varies considerably. It is least favorable in those cases which show absolutely no organic manifestation. As far as psychotherapy is concerned, in the mild cases, simple suggestion seems best; in the severer cases, formal psychotherapy and in the most severe cases, as in the case of persistent hymen over many years in a psychopathic person, "*noli me tangere*."

Training in psychoanalysis has a triple usefulness in the treatment of these cases: (1) It offers the road to the possible understanding of the complex mechanisms through which these conditions arise. (2) It

offers a technic for intelligent listening in the eliciting of an adequate history. (3) In very carefully selected cases, it offers a radical therapy which attempt to combine the removal of symptoms with an adjustment or readjustment of an unhappy individual.

1150 FIFTH AVENUE.

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## A CASE OF MARKED HYDRAMNIOS IN THE FIFTH MONTH OF PREGNANCY\*

E. EVERETT BUNZEL, M.D., NEW YORK, N. Y.

MRS. W. P. B., aged twenty-six, white, was seen by me in her first pregnancy in July, 1926. Her menstrual history had always been normal of the twenty-eight day type. Her past history had been insignificant except for measles as a child and an appendectomy in 1918. Her expected date of confinement was estimated to be about February 24, 1927.

At seven months, an external cephalic version was done. She was delivered at term by low forceps of a 7 pound 14 ounce baby girl, after a labor of seventeen and one-half hours. She made an uneventful recovery, nursing the baby several months.

On November 4, 1931, she came to consult me in her third pregnancy, having had another baby girl in September, 1930. This pregnancy was normal, the labor short and easy, and this baby weighed 7 pounds 14 ounces also. Although she nursed for seven months, up to April, 1931, she menstruated regularly after the first two months. Her last period began on May 25, and lasted the usual five days. Therefore at the time she came to me she had just completed the fifth month of her third pregnancy.

In the early months of this pregnancy, as with the other two, she had mild nausea and vomiting and under the care of a local physician out of town, noticed nothing unusual until the middle part of her fourth month. At this time both she and the doctor thought her abdomen was larger than it should be for the period of gestation. The uterus from that time on continued to grow rapidly in size and the patient had increasingly severe backache and discomfort, to such a marked degree that she was unable to sleep well even propped up in bed and with three allonal tablets at bedtime. She had felt life on October 16 (at four and one-third months).

On physical examination on November 4, her face was flushed, her eyes sunken; she looked tired, and her hands were bluish in color. The abdomen appeared to be the size of a full term pregnancy or more. The skin of the abdominal wall was suffused, and blanched on touching it. It was impossible definitely to outline the uterus as it was flaccid and occupied the entire abdominal cavity, but there was a distinct fluid wave throughout. The abdomen measured 106 cm. in diameter at the level of the navel. No fetus or fetal parts could be palpated, nor could a fetal heart be heard. However, I could hear fetal movements. The lungs and heart were normal and the blood pressure 108/70. Mouth temperature was 99° and pulse 130. The cervix was soft,  $\frac{3}{4}$  of an inch long and admitted only the tip of a finger. No presenting part could be felt. A diagnosis of acute hydramnios was made.

I advised admission to the hospital at once because of the patient's extreme discomfort. A blood count showed: Red blood cells 3,730,000, hemoglobin 74, white blood cells 10,200, polymorphonuclear leucocytes 83 per cent. Blood was Type 1 (Jansky).

X-ray of the abdomen done the afternoon of admission, November 4, 1931, was somewhat indistinct because of the hydramnios, but a good film was obtained the next morning with the following report: "Films of the abdomen demonstrate an

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\*Read at a meeting of the New York Obstetrical Society, January 12, 1932.

enlarged uterine shadow suggesting polyhydramnios. Within the shadow of the uterus we see a single fetal skeleton. The size is greatly out of proportion to that of the uterus. We see no evidence of fetal anomaly. The size of the fetal shadow suggests a four to five months' pregnancy."

The problem at this time therefore, was to determine if it would be possible to comfort the patient sufficiently to permit continuation of the pregnancy. But repeated doses of morphia and luminal, given hypodermically, were without sufficient effect to justify this procedure. The abdominal discomfort, backache and dyspnea were so marked that the patient had to be propped up in bed almost into an erect position. And in addition she could not sleep. Therefore after forty-eight hours' trial it was decided to interrupt the pregnancy.

On November 6, 1931, under nitrous oxide because of the patient's nervousness and apprehension, and after preparation of the vulva and vagina with iodine and catheterization of the bladder, pelvic examination showed the cervix to be soft, about  $\frac{1}{2}$  inch in length and readily admitting a finger through the internal os. The cervix was gradually dilated until two fingers could be introduced. A stilette was then passed through the cervix and the membranes were ruptured high up at 9:40 A.M. Keeping two fingers in the cervix, the amniotic fluid was allowed to drain off very slowly over a period of fifty minutes. During this time, the uterus began to contract irregularly, and the patient's pulse dropped from 128 to 100 at which level it remained throughout the labor. The measured amount of amniotic fluid was 11 quarts. After complete drainage the abdomen was tightly bound. The contractions continued irregularly, and at 11:30 A.M., one hour later, there was a sudden gush of blood per vaginam completely saturating the vulval towel. From this time on, there was a small amount of oozing of blood from the vagina. Three doses of pituitrin were given of minims three, four, and five at 12:30, 1:00, and 2:15 P.M. respectively until the uterine contractions were definitely regularly established. Eventually, a vertex presented completely covered with membranes. These were ruptured and a very small amount of amniotic fluid escaped. The fetus was delivered at 6:11 P.M. and two minutes later came another fetus by the breech, considerably smaller than the first. The second fetus was markedly discolored and the cord of the second fetus was very much smaller than that of the first. There was very little bleeding after the birth of the fetuses, but the uterus had little tone to it and did not contract well.

At the end of half an hour, the operator's hand was introduced into the uterine cavity and 1 placenta with 2 sacs was removed, and although there was no marked bleeding at this time, but because of continued relaxation of the uterus, iodoform packing was introduced into the uterine cavity and vagina.

While under the anesthetic at the time of rupturing the membranes, a specimen of venous blood was taken: The blood Wassermann was later reported negative and the blood sugar 83 mg. Examination of the amniotic fluid showed a specific gravity of 1.002, no sugar, and the cell count was 135 leucocytes per cubic mm.

Fetus A, female, was 28 cm. in length and weighed 17 ounces; fetus B, also female, was 16 cm. long and weighed 8 ounces; neither fetus was macerated though both were stillborn.

The smaller fetus was within the amniotic sac containing the excessive liquor amnii. The single placenta with two sacs appeared normal grossly but unfortunately, microscopic study of the placenta and autopsies of the babies were not done.

The patient's convalescence was uneventful and afebrile, the vaginal and uterine packing being removed twenty-two hours after delivery. She was discharged from the hospital on the 14th day in excellent condition and feeling well. Prior to discharge a chest x-ray was done which reported nothing to suggest tuberculous infiltration and the heart shadow appeared normal.

The follow-up examination made on January 5, 1932 (two months after delivery) found the patient in splendid general condition. The abdominal wall was lax and

showed marked striations. The pelvic floor was slightly relaxed; the uterus was in normal anterior position; the adnexa were normal, and the cervix showed bilateral lacerations without erosion.

215 EAST SEVENTY-SECOND STREET.

(For discussion, see page 784.)

## REPORT OF A CASE OF SIX MONTHS' UNRUPTURED ISTHMIAL TUBAL PREGNANCY

HERSCHEL HEINZ, M.D., NEW BEDFORD, MASS.

(From the Obstetrical Service, St. Luke's Hospital)

A PREGNANCY actively developing for about six months, without bleeding or rupture, in an ovisac consisting solely of a markedly hypertrophied fallopian tube is an unusual occurrence. Cases partly analogous in one respect or another are to be found in the literature but none exactly comparable to this one, for which reason I report it in some detail.

The patient, a French woman of twenty-seven, was admitted to the obstetric service of St. Luke's Hospital on the fifth of September, 1931.

Her chief complaint was of intermittent pain of one month's duration, the pain being referable to the lower abdomen.

The present illness began with the cessation of menses on March 11, 1931. Believing herself to be pregnant, the patient consulted her family physician for prenatal care. For four months nothing unusual was noted by either the patient or her physician. After this period the patient remarked upon the absence of any signs of fetal life. Continued observation at no time revealed fetal movements or fetal heart sounds. The growth, however, of what was supposed to be the pregnant uterus was perfectly normal and consistent with a normally progressing pregnancy.

For a month before hospital entry the patient complained of intermittent lower abdominal pain at times accompanied by nausea and vomiting and occasionally of sufficient severity as to require the administration of morphia. The examination of the abdomen by the family physician at the time of these attacks disclosed no apparent intra-abdominal pathology. Two weeks before entry the blood pressure began to rise. During the forty-eight hours previous to admission the systolic pressure rose from 160 to 208. The blood pressure in two previous pregnancies had never been over 120. The present illness was unaccompanied by fever, bowel or urinary disturbance, or any evidence of bleeding, either external or internal.

The past history was essentially negative. The patient had had two normal pregnancies terminating by low forceps. The menses previous to the present illness had been regular, of the twenty-eight day type. The flow was moderate in amount, of normal character, and of four to five days' duration. The patient's last period was normal in every respect. There was no history of dysmenorrhea, intermenstrual bleeding or vaginal discharge. No history of venereal disease could be obtained from either the patient or her husband.

The patient was a fairly well developed and nourished woman apparently in moderate pain. The color was good. Temperature 99.4° F., pulse 88, and respirations 20. The blood pressure was 208 over 134.

The general physical examination was negative except for the presence of marked dental caries. The breasts were full and somewhat sensitive, consistent with the mammary enlargement of pregnancy.

Abdominal examination revealed the presence of a smoothly globular, freely movable mass, reaching to, or a little above the umbilicus with the patient in a reclining position. This mass was firm and tense, resembling in feel the uterus in a case of ablatio placentae. It was somewhat tender to pressure. During the examination the

patient complained of continuous lower abdominal pain. No contractions or relaxations of the mass could be observed. The abdominal examination was otherwise without significance.

Vaginal examination showed a slightly violet-tinged mucous membrane. The cervix was in normal position, small, and much firmer than one would expect in a multiparous woman. Hegar's sign was absent. The os was about one-half cm. in diameter. Movements of the mass were reflected only slightly in the cervix, the two apparently not intimately connected. To the right of the midline a smaller mass could vaguely be felt by bimanual palpation and this seemed to be more closely associated with the cervix. The examination was otherwise negative.

The urine showed a very large trace of albumin with an occasional granular cast. A roentgenogram was reported negative for pregnancy but later was stated to have been incorrectly exposed.

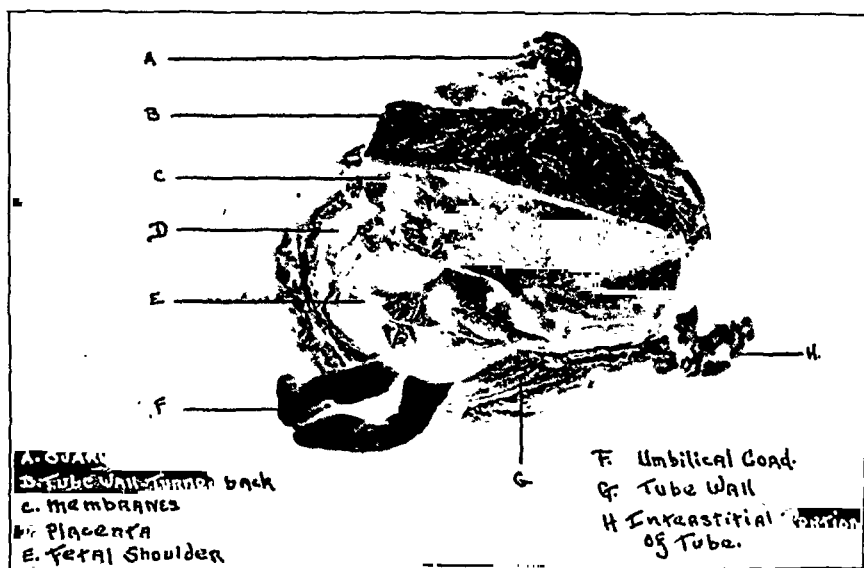


Fig. 1

The diagnosis presented obvious difficulties. The possibility of a rudimentary horn pregnancy was considered. In view of the pain, rising blood pressure, and the character of the mass it was considered advisable to do an immediate laparotomy.

The operation was performed under novocaine spinal anesthesia, the abdomen being opened by a midline incision from pubis to umbilicus. On opening the peritoneal cavity the mass was found to be a freely movable tumor lying approximately in the midline. It had the appearance of a normal six months' pregnant uterus. With good exposure, however, it was readily seen that the mass was tubal in origin. The uterine attachment of the left tube was hypertrophied and about two centimeters in diameter gradually swelling to form a tumor somewhat larger than a good sized grapefruit. The left broad ligament was proportionately widened and full of dilated, tortuous blood vessels. The ampullary end of the left tube and the left ovary arose from the posterior surface of the tumor and were intimately attached thereto. The sigmoid was loosely adherent over a small area on the posterior surface of the tubal mass. There was no blood or exudate in the pelvis nor any evidence of previous bleeding.

The uterus was displaced slightly to the right of the midline and was enlarged approximately to the size of a two months' pregnancy. The right tube and ovary were normal and free.

The sigmoid was easily dissected free of the tube. The left mesosalpinx was divided between clamps and the tube resected from the uterus by a wedge-shaped in-

cision. All bleeding and raw surfaces were then sutured with No. 2 chromic catgut, and a routine appendectomy was performed after which the abdomen was closed in layers without drainage. The patient left the operating room in excellent condition. Her convalescence was smooth and uneventful, the maximum temperature being 100° F., on two occasions only. Twenty-four hours after operation the blood pressure was 140 over 110, and on September 18 when the patient left the hospital, it had reached a normal of 122/84. The urine examination on discharge was negative.

The excised tubal mass was opened by a short incision, with an immediate gush of clear amniotic fluid and the extrusion of an umbilical cord about three-quarters of a centimeter in diameter. (Fig. 1.) The wall of the tube in its central portion was one centimeter in thickness. The specimen was placed immediately in "Museum" fluid, pending examination by our pathologist. This caused some shrinking so that measurements made at a later date are somewhat smaller than those made at the time of operation.

The fetus was well preserved and although the fetal heart was not beating it was quite evident that life had been present up to within a short time of the operation. The embryo, a female, was perfectly developed and weighed 375 grams. Its crown-rump length was 16 centimeters, crown-heel length 25.5 centimeters.

The measurements and the weight of the fetus show its development to be between five and six months which checks well with the period of pregnancy as calculated from the date of the last menstrual period. It is to be assumed that the growth of the fetus must necessarily have been retarded by the restricted space in which it was developing.

An x-ray of the tubal mass taken after its removal from the abdomen showed the skeletal structure of the fetus, the development being normal for its apparent age.

The examination of the specimen was made by our pathologist, Dr. Isabel M. Wason, whose report is as follows:

*Gross.*—The specimen consisted of a large round tubal mass and an ovary. The mass, which measured 12 by 10 by 9 cm., was in the middle portion of the tube with the short tubal pedicle on one side and on the other approximately 2 cm. of tube ending in a fimbriated extremity. This mass had been opened revealing a fetus, cord, and placenta which was still attached to the wall. Membrane could be peeled away from the inner wall. Muscle composed the greater portion of the wall which was 6 to 8 mm. thick.

The fetus has already been described.

The ovary measured 3 by 2 by 1.5 cm. It was firm and contained a corpus luteum which comprised about half its mass.

*Microscopic.*—Tube: Sections taken from the pedicle showed the structure of the proximal portion of the fallopian tube, with empty lumen and broad folds covered by intact epithelium. In the distal end the folds were thin with free tips and were covered by well-preserved epithelium. Only a few scattered small monocytes appeared in the folds and walls. The outer walls of the mass in the central portion consisted of hypertrophied smooth muscle fibers. The inner wall showed sheets of syncytial cells and chorionic villae. Part of the decidua was necrotic and a few polynuclear and mononuclear cells invaded the wall beneath. The chorionic villae were covered by a single layer of epithelium.

The ovary contained a well-developed corpus luteum. No undeveloped follicles were seen in the sections but there were a number of hyaline scars.

#### DISCUSSION

An unusual case of ectopic pregnancy is presented.

Certain interesting features of this case which manifest themselves are:

First, the degree of hypertrophy undergone by the tube. It is remarkable that this could have occurred in a structure not ordinarily thought of as a muscular or very distensible organ.

Second, the absence of involvement of any pelvic structures other than the tube in the formation of the ovisac.

Third, the apparently normal development of the fetus which was probably not arrested until shortly before the patient entered the hospital. The amount of subcutaneous tissue was somewhat less than is normal for a corresponding period of intra-uterine development but this is to be expected from the limited space occupied by the growing fetus.

Fourth, the rise of blood pressure and beginning kidney pathology without subjective symptoms, both responding promptly to the termination of the pregnancy without specific treatment. One may conjecture that this manifestation of toxemia is analogous to that seen in cases of multiple pregnancy, polyhydramnios, and allied conditions.

7 NORTH ORCHARD STREET.

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## CANCER OF THE VULVA IN YOUNG WOMEN\*

HYMAN STRAUSS, M.D., BROOKLYN, N. Y.

(Assistant Visiting Surgeon, Brooklyn Cancer Institute)

CANCER of the vulva is relatively rare in young women. The earliest case reported was found to be that of a young girl of fourteen years, by Kinoshita, and a woman twenty years of age, by Ossing.†

Taussig reports cases of vulvar carcinoma in two women, one twenty-seven and the other thirty-three years of age. The Mayo clinic has reported no case of a patient under thirty years of age.

CASE 1.—B. K., white, aged twenty-two, born in U. S. A., married, but never pregnant. Patient was in very good health until the onset of present illness in September, 1930. At this time she noted an inflammation of the right labium majus, for which she used several ointments. The lesion ulcerated in a short time, and she consulted a doctor who advised continuation of the salves. As the inguinal nodes on the right side became involved, she developed pain in right side and groin. Two months later, the local lesion was cauterized. After a few weeks the lesion recurred. A blood Wassermann at this time proved negative. No loss of weight occurred. The patient entered a local hospital where a biopsy was taken. The pathologist's report of this was:

*Microscopic examination* showed the normal tissues to be largely replaced by a squamous cell epithelioma composed of nests, columns, and more diffuse masses of pavement epithelium supported by relatively sparse fibrous stroma which was well vascularized and densely infiltrated with inflammatory cells, most of which were of the lymphocytic variety. The neoplastic epithelium in places was well differentiated and showed cornification and pearl formation. In other places the cells were more or less anaplastic and many of them exhibited mitotic figures. In several areas, the tumor was seen to arise from the pavement epithelium covering the surface of the vulva. In other areas, the surface showed necrosis or ulceration.

*Diagnosis.*—Squamous cell epithelioma of the vulva.

The local lesion was coagulated with the high frequency current. The inguinal glands were not treated. On February 21, 1931, she was admitted to the Brooklyn Cancer Institute; she weighed 103 pounds. She had a slight leucorrhea, no urologic symptoms, her menstrual history was negative. The internal genitalia were nega-

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\*From Division of Cancer, Department of Hospitals, New York City.

†Since this paper was written, a case of melanosarcoma in a girl of seventeen was reported by Healy at the Brooklyn Gynecological Society on December 4, 1931.

In a personal communication to the author, Dr. Neill, of the Howard Kelly clinic reports treating a cancer of the vagina in a girl sixteen years of age.

tive. There was a slight leucorrhea which could not be explained by any physical findings. The right labium majus and minus were markedly hypertrophied. The superficial epithelium was desquamated. In the center of this area of desquamation, and definitely away from Bartholin's duct, there was an ulceration 2 cm. in diameter. The edges of the ulcer were indurated, elevated and rolled. There was a marked secondary infection which caused the lesion to be exquisitely tender. The opposite labia were normal in all respects. There was present a moderate serosanguinous discharge. The inguinal glands on the right were enlarged but not ulcerated. The glands in the left groin were barely palpable. There was slight amount of pain in the right thigh.

X-rays showed no metastasis in lungs or bony pelvis. Blood count showed hemoglobin 70 per cent, type 2, R.B.C. 2,490,000 normal cells, W.B.C. 9,600, Polymorphonuclears 80 per cent. Treatment was begun with deep x-ray therapy to the pelvis. The high voltage x-ray cycle consisted of the following factors: 5 ports, 2 anterior, 2 posterior, 1 perineal, size 20 by 20 cm., 50 cm. distance, 180 kv., 4 ma. Filtration,  $\frac{1}{2}$  mm. copper and 1 mm. aluminum. 215 R units to each port. This was repeated every second day until six treatments were given. The average patient is about 8 inches thick. Over one-half the radiation intensity therefore, reached the mid-pelvis, which received 62½ per cent of a S.E.D. at each sitting.

On March 25, under avertin anesthesia, 15 platinum needles were implanted around the vulvar lesion. The following factors were involved: Applicator, 15 platinum needles 35 mm. long; content, 2½ mc. radon each; filtration, 0.5 mm. platinum; duration, five days and four hours; dosage, 3000 mc. hours. Ten days later, another x-ray cycle was administered. The right inguinal glands became infected and fluctuant, and were incised and drained. The area of ulceration on the vulva subsided slightly. The patient's general condition improved to a slight extent. It was decided to radiate the inguinal gland, as we felt that the infection was well walled off. A tube of radon was applied to this area. The following factors were involved: Applicator, 1 platinum tube; contents, 10 mc. radon; filtration, 1 mm. platinum; duration, four days and five hours; dosage, 700 mc. hours. The glands in the left groin enlarged, and gradually became definitely involved in the spreading process.

Two months later, the patient was discharged to a convalescent home, and later received a repetition of the x-ray therapy. The disease, however, progressed, and the patient reentered the hospital, at which time examination showed one lymph node in the right groin the size of an egg, red, tense, and tender. The other nodes on both sides had ulcerated, the vulvar lesion had extended to the mons veneris, and ulcerated the adjacent tissue and spread to the left labia. The blood study showed a moderate anemia. X-ray of lung and bony pelvis still negative. Patient became extremely weak and emaciated. She had a profuse hemorrhage from the right inguinal lesion which was controlled by packing. At no time did the patient have edema or varicosities of the legs. The suprapubic ulceration extended to the bladder which was exposed, as was the rectus muscle and the pubic bone. Both groins broke down, and ulcerated very extensively, exposing the fascia lata and the external iliac vessels. Her condition became progressively worse, and on August 5, 1931, she died. No autopsy was obtained.

CASE 2.—F. R., a negress, aged twenty-nine, widowed, and mother of one child. General condition good until present illness. Definite history of syphilis.

About July, 1929, the present illness started as an itch of the vulva which was treated with blue ointment, lysol locally, and lysol douching. A pimple developed which she squeezed. At this time she was told that her blood was bad, but she neglected to take treatment for a year. She entered a local hospital in June, 1930, complaining of a hard mass involving both labia majora and infiltrating the tissues, extending into the vagina. The clitoris was also involved. There was no involvement of the inguinal lymph glands. Spinal Wassermann was negative. Biopsy was taken and reported as follows:



*Microscopic Examination.*—The section showed mucous membrane and underlying submucosa. There was a marked hyperplasia of the stratified squamous epithelial cells of the mucosa and the basal cells showed marked pigmentation by melanin. Invading the submucosa in rather irregular islands and torturous columns were found epithelial cells derived evidently from the overlying mucosa. The invasion was rather disorderly in character and the differentiation was fairly well marked. The remainder of the submucosa was densely invaded by polyblasts.

*Diagnosis.*—Epidermoid carcinoma.

This patient received six injections of 0.6 neoarsphenamine and eight intramuscular injections of 1 c.c. of bismogenol, Wassermann was 2 plus. She was referred to the Brooklyn Cancer Institute where she received a course of high voltage x-rays to the pelvis, consisting of the following factors: 5 ports, 2 anterior, 2 posterior; 1 perineal, size 20 by 20 cm.; 50 cm. distance; 180 kv.; 4 ma; filtration,  $\frac{1}{2}$  mm. copper and 1 mm. aluminum; 215 R units to each port. This was repeated every second day until six treatments were given. The average patient is about 8 inches thick. Over one-half the radiation intensity, therefore, reached the midpelvis, which received 62½ per cent of a S.E.D. at each sitting.

On September 15, 1930, she was hospitalized; she weighed 99 pounds. She had no urologic symptoms. Spinal fluid gave a negative Wassermann, while blood was three-plus. Blood chemistry normal. Blood count, red blood cells 4,180,000, white blood cells 4,000, Polymorphonuclears 70 per cent, hemoglobin 60 per cent. Vaginal examination showed vagina, cervix, uterus, and adnexa normal. There was marked ulceration from the symphysis pubis extending into the vagina. The ulcerated area was about one inch wide, exposing the pubic bones. The edges were ragged and bleeding, the inguinal glands were enlarged.

While in the hospital, she received a radium treatment of 3000 mch. distributed in 18 tubes of 10 mc. radon each, placed on a wax mold 1 cm. distance from the lesion, over a period of eighteen hours. Each tube was filtered by 1 mm. of platinum. The following week, patient received an additional 3000 mch. The factors involved were eighteen needles of platinum, 35 mm. long, and 5 mm. thick containing 2 mc. radon each, and these were placed by puncture around the growing margin for five days and eight hours.

On September 28, 1930, the patient left the hospital against advice. On January 17, she was again admitted to the hospital where she was originally treated. Her general condition was much worse. Her body was mere skin and bones, and she had a general glandular enlargement. The interne described the lesion as a "large ulcerated area about the vulva, clitoris, and inguinal regions, from which a horrible stench issues forth." Two blood Wassermann tests proved negative. In spite of local treatment with Carrell-Dakin solution, and Bland's pills by mouth, she became much worse.

Again she was transferred by ambulance to the Brooklyn Cancer Institute on July 24, 1931. Her admission blood study revealed negative Wassermann, hemoglobin 20 per cent, R.B.C. 1,620,000, with marked anisocytosis and poikocytosis. The W.B.C. were 3,970 with 73 per cent polymorphonuclears.

X-ray at this time showed destruction of portions of the pubic bones and ischial rami. She complained of severe vulvar and lower abdominal pain with intense burning of the genitalia. The pubic bone was exposed, the bladder wall was visible, the mons veneris was gone, and all the landmarks were gradually lost. The area of destruction extended up the anterior abdominal wall, midway between the pubis and the umbilicus, and posteriorly as far as the anal orifice. This entire lesion was fungating, sloughing, bleeding, discharging, and foul smelling. The legs never developed edema or varicosities. The cachexia increased, she became irrational, and on August 17, 1931, she died. Autopsy permission was refused.

# Society Transactions

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## AMERICAN GYNECOLOGICAL SOCIETY

### FIFTY-SEVENTH ANNUAL MEETING

Quebec, Canada

MAY 30, 31, AND JUNE 1, 1932

The following papers were presented:

**The Present Position of Version and Extraction**, Drs. Joseph L. Baer, Ralph A. Reis, and James J. Lutz, Chicago, Ill. (See page 599, October issue.)

### DISCUSSION

DR. PHILIP F. WILLIAMS, PHILADELPHIA, PA.—In a survey made in 1931, by a Philadelphia committee on maternal mortality in that city, out of 33,000 deliveries, 23,000 occurred in 53 hospitals during the year. Among these were 359 versions and extractions, an incidence of 1.5 per cent, which is twice as high as that given by Dr. Baer. Version and extraction is therefore being used to a considerable degree in Philadelphia. Out of 23,000 women, confined in hospitals, 4,800 were delivered by forceps, of which 187 were high operations, an incidence of 0.37 per cent. There were 576 cesarean sections, an incidence of 2.6 per cent. High forceps would therefore seem to be almost a negligible operation in Philadelphia. Version and extraction still retain a fair place in operative obstetrics. I believe that the mortality following version was much lower proportionately than from high forceps and very definitely lower than it was following the 576 cesarean sections.

DR. ALFRED C. BECK, BROOKLYN, N. Y.—In our clinic in Brooklyn we follow very much the outline recommended by Dr. Baer. We have found, however, an additional aid in the use of the abdominal binder during the second stage. Since we have been using this routinely, the need for any of these three procedures has been very greatly diminished. We also teach our students to give more regard to the first stage of labor, so that when the patient reaches the second stage she will be strong enough to make the binder of value.

DR. J. M. BERGLAND, BALTIMORE, MD.—At the Johns Hopkins Hospital during the past year we have done very few versions and extractions and, I am glad to say, extremely few high forceps. We appreciate the difficulties of these procedures, and as opportunities for doing versions and extractions are becoming fewer, we feel that our skill in doing this operation in a satisfactory way is diminishing. However I believe that probably we are not doing as many versions and extractions as we should do. We follow the technic of Potter as nearly as possible, and I believe that his suggestions for the performance of the actual operation are valuable; on the other hand, I am sure that one of the most important things done in our Clinic during the last year has been the liberalization of the indications for cesarean section.

DR. EDMUND B. PIPER, PHILADELPHIA, PA.—I would like to make one possible criticism regarding the question of terminology and the word "elective." In our teaching at the University we use three indications for podalic version; first, the routine cases; second, elective; and third, emergencies. We only use the term "emergency version" where it is done in the presence of failing fetal heart sounds, but we use elective version when there is a choice between version and forceps.

I believe that podalic version is one of the most difficult, if not the most difficult, operation in obstetrics.

DR. BAER (closing).—Dr. Williams emphasized a point, namely that we had not given version and extraction its proper place in these last five years. His figures are about what should be and which we are now hoping to attain.

Dr. Beck's comment about the value of the abdominal binder in the second stage of labor is a highly important one. If the patient is a multipara with a pendulous, grossly relaxed abdomen, I regard the binder as definitely desirable. I am not yet convinced that for the normally sound abdominal wall the binder is anything more than perhaps a handicap to proper observation of the heart tones during the second stage. So, except where specifically indicated, we do not use it.

With reference to my misuse of the word "elective," what I had in mind, of course, was the "routine" or Potter type of version and extraction and Dr. Piper's comment was entirely justifiable. Version and extraction may be routine, elective, or emergency.

I cannot feel that version and extraction should be characterized as essentially a difficult operation. I do believe we should emphasize that the trained obstetrician should know how to do version and extraction. If he possessed that knowledge and skill, then I regard it as a comparatively simple procedure in the suitably selected patient, and I rather deprecate the position that version and extraction should be labeled by this Society as one of the most difficult of operations.

**A New Axis-Traction Forceps, Dr. Edmund B. Piper, Philadelphia, Pa.**  
(See page 625, October issue.)

#### DISCUSSION

DR. NORRIS W. VAUX, PHILADELPHIA, PA.—First, a word of warning about Dr. Piper's forceps, the model he has just now presented. It is a very dangerous forceps because the force of the axis-tractor is tremendous if not applied properly. With care, this instrument needs very little traction, and if too much force is applied, there may be very extensive internal and external injuries, accompanied by profuse hemorrhage, and from lacerations occurring in the improper use of any type of forceps. The warning is not to pull too vigorously but rather very cautiously throughout the operation. This instrument is used quite routinely in our service. It also can be applied to the after-coming head quite as simply as the forceps previously devised by Dr. Piper for this purpose.

DR. WILLIAM E. CALDWELL, NEW YORK CITY.—We have used his forceps at the Sloane Hospital for Women for several months. It has given very satisfactory results, making all types of operation simpler.

The instrument is well made, the fenestra nicely cushioned; there is a considerable spring to the blades which prevents excessive pressure although holding the head nicely; the curve of the shank gives excellent axis-traction. The forceps resemble greatly the Lusk modification of Tarnier's original forceps. Although the axis-traction principle was developed for use when the head was high in the pelvis, especially for high forceps, it is the proper maneuver anywhere in the pelvis, even for low forceps.

In rotating the head we agree with Bill that it should be rotated in the planes of the greatest diameter, preferably by hand, if necessary with a solid blade forceps or the Barton instrument. Dr. Piper's forceps have to be handled with great care and skill when used as rotators.

DR. JOSEPH B. DELEE, CHICAGO, ILL.—I would like to condemn all axis-traction forceps, not particularly Dr. Piper's or Tarnier's, on the grounds that the axis-traction forceps is not artistic. One simply applies a big heavy pair of tongs

and then pulls and the soft parts and the pelvis force the direction in which the head has to move. As the last speaker has shown, the axis-traction forceps cannot be used for rotation.

Dr. Piper stated that I preach the use of single forceps for all work. That is true for the general practitioner, but there are two forceps on the market which are useful in certain conditions, in the hands of the expert, the Kielland and Barton's forceps. I have used the latter simply for the purpose of pulling the head into the inlet when the head lies high in the transverse diameter. For that purpose I think it is the best instrument that we possess today. After the head has been brought down into the pelvis the Barton forceps is removed and the rest of the operation completed with manual rotation, aided if needed by the Simpson forceps. I think the use of high forceps should be limited in favor of version. In difficult cases where the axis-traction forceps would be used, the delivery could be probably better effected by version and extraction.

I can imagine a case where the head is packed into the pelvis and where brute force applied with the axis-traction instrument would be necessary. Dr. Rubowitz has invented the term "precraniotomy forceps" and I think that is a good name for those high forceps operations done in the tender hope of getting a live baby when the only alternative is craniotomy. Craniotomy is a rare operation and getting less necessary all the time. I would call attention to the fact that the obstetrician still has a pair of hands and has eyes at the end of his fingers, and that aided by a study of the mechanism of labor he can use the Simpson forceps in practically all of the cases where it is necessary to make an instrumental delivery.

DR. WILLIAM B. HENDRY, TORONTO, CANADA.—In Toronto we have been confused by the profusion of the types of forceps on the market to such an extent that one of the junior members of our staff has undertaken to make a forceps which would combine the good qualities and have none of the defects of all the forceps. We are inclined to think that probably he has succeeded in this. The principle of his forceps depends upon being able to split a universal joint, which enables one, without removing the forceps after it is once applied, to perform the operation of bringing the head into the pelvis, doing a rotation and also an extraction.

DR. PIPER (closing).—Just to reiterate the last sentence of my paper, I made those forceps to suit myself, and it does not interest me particularly whether anybody else likes them or not.

I agree with Dr. Caldwell that rotation of a head with any instrument is a difficult and dangerous procedure.

Dr. DeLee said that no axis-traction forceps should be used. He does not do high forceps very often, which might explain the rather high incidence of elective cesarean section in that clinic.

I wish I were able to do without an axis-traction forceps. I wish I could deliver a baby as Dr. DeLee does, but I cannot, and I want to get the forceps that makes it as easy as possible without injuring the baby and the mother, which I can do readily with these forceps I have exhibited.

**Twelve Years' Experience With Uterotubal Insufflation: Diagnostic and Therapeutic, Dr. I. C. Rubin, New York City. (See page 561, October issue.)**

#### DISCUSSION

DR. NORMAN F. MILLER, ANN ARBOR, MICH.—To maintain a permanent place in medical practice every diagnostic test must meet certain qualifications. It must be safe; it must give sufficient information to warrant its use; and it should not be technically difficult.

Dr. Rubin has shown that if proper precautions are taken his test is practically without morbidity. My own observation and experience would tend to substantiate this. No serious complication occurred in over 400 tubal insufflations at the University of Michigan. Only in one case have I seen high fever and signs of pelvic inflammation following the test. The indications, requirements, and contraindications laid down by Dr. Rubin are based on long experience and the analysis of abundant clinical data. They should serve as standards, and any competent physician willing to observe these rules may use the test with safety.

Does the test give sufficient information to warrant its routine use? The answer is obvious. If it gave only half as much information I would still consider it a necessary procedure in every study of sterility. Indeed, it is no longer simply a tubal patency test because in its present highly developed form it is possible to obtain much additional information. For instance, spasm, partial, or complete stricture of the tube and its probable location may be determined by tubal insufflation with kymographic attachment. As a diagnostic procedure it is not only safe but indispensable in the study of sterility.

I must confess, however, that my preference lies in the use of opaque substances injected under controlling fluoroscopic examination. By this method we learn just as much concerning tubal patency, and we obtain a better idea as to the character and location of tubal stricture or obstruction. If plates are taken at the time of injection and again within twenty-four hours a more desirable permanent record of the condition of the tubes is obtained. Furthermore, I have greater confidence in the findings demonstrated by this method. Dr. Rubin reported nearly 7 per cent of morbidity following the use of opaque substances. This seems very high. As yet, I have seen no untoward results from the employment of oil, but I perhaps shall go back to CO<sub>2</sub> after reading Dr. Rubin's forthcoming monograph on the use of opaque substances.

So far as the third qualification is concerned the technical difficulties of the test are certainly no obstacle to its use. In this respect it is superior to the injection of opaque materials. The use of x-ray often means inconvenience as well as added expense, both of which are important drawbacks to oil injection as a routine procedure.

The therapeutic value of tubal insufflation is as significant as it is spectacular.

The fact that 66.6 per cent of 57 dysmenorrhea patients were relieved following the test certainly warrants further study. To my knowledge few remedies or therapeutic measures can surpass this record.

Just how much time may lapse between the test and subsequent pregnancy in order to justify attributing the result to the test is perhaps open to discussion. It seems to me, however, that Dr. Rubin is very fair and conservative when he states that "pregnancy must follow within a month or at least two months after insufflation."

That uterotubal tonicity is increased during the tenth to the sixteenth day of the menstrual cycle and decreased in functional amenorrhea of young women, is in my opinion, a most interesting observation. This would appear to support the views on tubal propulsion of the ovum.

I should like to ask Dr. Rubin what significance he attaches to the fact that 60.46 per cent of tubal obstructions followed appendicitis? Even though the right tube be involved one would not expect so many closures on the left side.

DR. N. SPROAT HEANEY, CHICAGO, ILL.—An analysis of 90 cases, in 1931, of pure sterility cases, i. e., cases which presented themselves for this chief reason, showed 60 per cent of the cases had absolutely normal tubes, 15 per cent were patent with some slowness and 24 per cent were absolutely closed. The patency test is of utmost importance when operating upon fibroids of the uterus in young women. If before the operation the tubes are found open, then the patient may

be told that there is a possibility of a myomectomy being done. If the tubes are closed, however, then a myomectomy would not be advisable for such an operation is only to be done to conserve childbearing, the chances of the recurrence of fibroids being great enough to forbid its use on the sterile woman.

DR. CHARLES C. NORRIS, PHILADELPHIA, PA.—A use for the Rubin test which was not mentioned by the essayist is occasionally found in those patients in whom it is desirable to employ intrauterine irradiation with radium for benign hemorrhages and in whom there is some question as to the condition of the tubes. Occasionally patients are encountered in whom palpation yields somewhat doubtful results and in these insufflation offers a valuable method of determining the condition of the tubes, for when these are not patent, radium is usually contraindicated.

DR. NATHAN SEARS, SYRACUSE, N. Y.—I would like to ask Dr. Rubin whether he considers it necessary to use x-ray as a routine or whether he can depend on the fluctuation of the monometer and the subsequent shoulder pain?

DR. RUBIN (closing).—In answer to Dr. Miller's question, about 60 per cent closure of tubes were found in appendicitis cases. Not infrequently, even in mild cases of appendicitis, there is a serous exudate in the pelvis, that results in cobweb adhesions implicating the left tube also. Where abscess formation takes place it also occupies the left side as well as the right.

Dr. Heaney was quite right about fibroids and tubal patency. I am accustomed to examine the tubes for patency in women still in the reproductive period of life who have fibroids and want to know whether a myomectomy can be done.

In reply to Dr. Sears, I have been in the habit of using the fluoroscope as a routine. I am still interested in the scientific check-up of all the data involved in the test; but the fluoroscope is not absolutely necessary. I think the kymograph and the shoulder pains give you all the necessary information. Where the kymograph is not available one can train himself to note the fluctuations of the mercury column. After a little practice one becomes adept at doing that and it is helpful.

The kymograph enables us not only to tell whether the tubes are patent but the degree of patency, i. e., whether they are normally patent, and if not normal, what kind of stenosis is present, and also whether there are peritubal adhesions or uterotubal spasm. In the vast majority of cases it is possible to locate the site of obstruction. The decision for or against operation to open the tubes is thus rendered possible and in this respect abdominal auscultation and careful notation of the sensory reactions during the insufflation examinations are important.

Another interesting thing to mention, as to the therapeutic action of insufflation, is that it was employed more than once in 247 of the 298 cases that became pregnant and in 27 per cent pregnancy followed within one month after the insufflation. That is a fair criterion if one wants to judge of its therapeutic value.

### **The Prophylactic Treatment of Thyroid Dysfunction and the Importance of Basal Metabolism Studies in Obstetrics and Gynecology,** Dr. Carl Henry Davis, Milwaukee, Wis. (See page 607, October issue.)

#### **DISCUSSION**

DR. WILLIAM C. DANFORTH, EVANSTON, ILL.—The use of thyroid in a good many obstetric and gynecologic cases is valuable and especially in hypothyroid conditions.

I believe there is a class of women who are more than normally inclined to abort who in the presence of a low basal rate are helped by the administrations of thyroid.

As to routine administration of iodine in all pregnant women, I would not agree. I have at the moment two women under my care who have been greatly benefited

by the administration of small doses of iodine but I would be rather hesitant about using iodine generally. I think the routine use of iodine may be of greater necessity in some regions of the world than in others and that should be taken into consideration. I have found that a very useful way of giving iodine is to use a saturated solution of sodium iodide. Patients seem to tolerate it over a considerable period of time. When the patient also has a moderate anemia, the iodide of iron has been found a very useful preparation.

DR. EDWARD A. SCHUMANN, PHILADELPHIA, PA.—I have been impressed by the importance of Dr. Davis' paper as applied to certain sections of the country and as opposed, if I may say so, to its lack of importance as regards other regions. Of course, as you all know, the entire area from the St. Lawrence Basin through the Great Lakes region, involving Wisconsin, Minnesota and that part of the West, was during the three glacial epochs under glaciers, and there were no iodine bearing flora or fauna developed in that region. On the Atlantic seaboard our incidence of goiter in infants is extremely low and I fail to recall a single case of congenital, rapidly developing goiter in my experience. Therefore, the necessity for routine stabilization of the thyroid is unimportant in the region from which I come.

I would disagree slightly with Dr. Davis in minimizing the danger of routine iodine administration. It is well known that about 8 per cent of all women between the ages of twenty and forty years possess possibly occult adenomas of the thyroid and while the routine administration of iodine may stabilize the thyroid output, it unquestionably stimulates adenomatous growth, and there have been a number of cases recorded of rapid development of the adenomas after the routine administration of iodine.

With regard to the use of thyroid extract, particularly in cases of sterility of unknown origin, I believe that this is a most important measure and I would point out the fact that apparently normal variations of the basal metabolism rate, minus 2 or 3 or 4 which fall within the normal reading, sometimes show the greatest clinical success upon the administration of fairly large doses of thyroid for a short period. I have had several instances of the empirical administration of thyroid in large doses with startling results.

DR. CAREY CULBERTSON, CHICAGO, ILL.—There is no condition in which the metabolic rate is more important to study than one to which Dr. Davis merely referred, that is, the climacteric. It was shown years ago that there is an instability of the blood pressure during this time of life, and we know that the basal metabolic rate is also disturbed. If that is so, it is difficult indeed during the climacteric years to evaluate accurately what is going on in individuals, whether they are developing hypo- or hyperthyroidism, and whether that condition is purely functional or is organic. I make these observations, because I have seen a number of patients in whom thyroid operations have been undertaken during the climacteric years, without any appreciable benefit whatever. I think this is a time when metabolism studies should be frequent and as accurate as possible. Too often the results obtained from such observations have been without avail, without any diminution in the symptomatology. We can group our climacteric cases into the hypo- and hypertensive types. The hypertensive cases have vasomotor disturbance and the hypotensive cases have symptoms suggesting hypothyroidism. The difficulty is in estimating how much of this condition is functional and how much is not. My experience has been that in the climacteric years the women will not be benefited by surgical therapy as the disturbance is usually transitory at the most.

DR. KARL M. WILSON, ROCHESTER, N. Y.—This problem which Dr. Davis presents is very important to us who live in the Great Lakes region. I would like to mention a prophylactic measure used in our community. Several times a year the whole water supply is iodinated with salts and that means, of course, that the whole

community gets the benefit from it whether they want it or not. Of course, that is no substitute for the careful study and observation of the individual patient, but I would like to point out that since that has been done in the past few years the incidence of congenital goiter has gone almost to the vanishing point, and goiter in school children has been reduced to about two-thirds of the usual number. Therefore, it is quite worth while. However, that would not be adequate treatment in a woman who shows a definite insufficiency.

DR. DAVIS (closing).—Fortunately Dr. Danforth is caring for a class of patients who from time to time go to the seashore. Most of his patients are traveling about more or less or get a considerable amount of seafood and therefore getting some iodine whether he gives it to them or not.

Dr. Schumann must take into consideration, I believe, the individual patient because patients who have been raised in goiter areas may from time to time migrate to Philadelphia, and if so it is very probable that if he is going to save the patient with a thyroid deficiency from developing children with an abnormal thyroid he must give that patient an adequate amount of iodine. Some may need small doses of desiccated thyroid in addition.

It is perfectly true that patients who are getting iodinated salt have in this country developed hyperthyroidism and toxic adenomas. But in view of the fact that all over Michigan, where the use of iodinated salt is compelled by law, the number of operations for toxic goiter has been greatly reduced, must be accepted as evidence that the use of iodinated salt has not increased the frequency of goiter. In Switzerland toxic goiter is practically unknown. They operate for cystic goiter and tumors of the thyroid but they do not have the type of toxic goiter which we see in this country. I feel that there is more and more evidence that the nervous system is responsible for the development of toxic conditions of the thyroid, and that it is not possible in view of our present manner of living for people with thyroid gland deficiency to avoid developing hyperthyroid states from time to time.

It is important to study these conditions in relation to the menopause, as Dr. Culbertson has pointed out, but it has been possible only to consider one phase of this subject today. I have tried to bring to your attention, with the hope of serious consideration, the importance of prophylactic treatment of thyroid disease as a means of preventing conditions which are easily prevented, and also suggest that we may in this way solve some of our other problems pertaining to the glands of internal secretion.

### **Results With Cordotomy for Relief of Intractable Pain Due to Carcinoma of the Pelvic Organs, Dr. Francis C. Grant, Philadelphia, Pa. (By Invitation.) (See page 620, October issue.)**

#### **DISCUSSION**

DR. FLOYD E. KEENE, PHILADELPHIA, PA.—Any procedure which gives promise of alleviating the sufferings of advanced carcinoma is worthy of serious consideration. Out of every 100 cases of cervical cancer the methods we employ are curative in only about 20 per cent, which means that in the remaining 80 per cent, the procedures used are at best only palliative. With the modern methods of irradiation, a large percentage of this incurable group will obtain at least temporary respite but in others, the response will be unsatisfactory, the pain will not be influenced and other measures must be used for relief.

The results which Dr. Grant has reported in his 25 cases of malignancy demonstrate beyond question of doubt the value of cordotomy. The relief from pain is usually not only complete but permanent, the procedure, when properly performed, is unattended by motor or functional disturbances and the patient's life is made



livable for the time that remains. The mortality of 16 per cent does not argue against the operation for, under such conditions, death is kind.

I am not sufficiently informed to discuss the relative merits of cordotomy as opposed to periarterial sympathectomy or excision of the presacral plexus. In a recent comprehensive review, Lorraine and Hermann reported results equal to Dr. Grant's and they assert that with the later procedures the technic is simpler, easier to acquire, that the operation is associated with no functional disturbance, and that the same operation enables one to verify the nature as well as the extent of the lesion. From the very limited experience which I have had in patients operated upon by Dr. Grant and Dr. Frazier, I believe that in a few properly selected cases, there is a definite place for these operations in the palliative treatment of extensive pelvic cancer, and that up to the present time, we have not taken advantage of the benefits which these operations may afford.

DR. RICHARD R. SMITH, GRAND RAPIDS, MICH.—I desire to give a brief account of the corresponding experience at our University of Michigan Hospital in the Division of Neurological Surgery. This department is in charge of Dr. Max Peet who with his associates, Dr. Kahn and Dr. Allen, has done 65 cordotomies. The number corresponds almost exactly with Dr. Grant's. Of these, 21 were done for carcinoma of the uterus, 3 for carcinoma of the prostate, and 4 for carcinoma of the rectum. Since we have only one object to attain, namely the eradication of pain, we may best form our judgment of the operation on the total number rather than upon those performed alone for malignancy arising in the pelvis. The results are much the same.

In 65 patients operated upon 50 gave satisfactory results. There were 4 cases the results of which were not determined and in 11 cases the results were unsatisfactory because of morphinism, the operation having been performed at too low a level, or because pain was not permanently eradicated.

Now we must bear in mind that the one object is to eradicate pain, very imperfectly controlled by the other means at our command, and if that can be accomplished we may put up with unpleasant experiences and complications, but it is well to bear in mind in the first place that we are usually operating upon patients who are hopelessly ill with all that the situation carries with it. There is also a considerable mortality. However, it is to be noted that mortality decreases with added experience.

Urinary disturbances (retention and incontinence) have been frequent and are a complication of some importance. In Dr. Peet's cases there were at least 22 patients who had marked bladder disturbance following operation. That is not taking into consideration the number that had such bladder disturbance before operation due to the invasion of the disease. We must remember, too, that good results are not always obtained. Pain has been known to recur after many months of relief for reasons not surely determined.

The technic must be very carefully and very exactly carried out, and I think we may hope for better results when there has been more experience with the operation. Certainly the experience of Dr. Grant in having practically perfect results in the last 18 cases is significant.

DR. GRANT (closing).—I am very glad that Dr. Keene brought up the question of section of the presacral nerve and the stripping of the internal iliac arteries for relief of pain from pelvic cancer, because there have been cases reported in the literature in which this procedure has been successful. Frankly, I have had no experience whatsoever with it. The latest and apparently the most authoritative report is that by Fontaine and Hermann (*Surg. Gynec. Obst.* 54: 133, 1932) who reports six cases of carcinoma of the pelvis, four of them having pain down the leg,

and in five of which the pain was completely relieved following this procedure. In the case in which pain was not relieved, the spread of the malignancy was so great that it was not possible to perform the operation they had in mind. The presacral tissue was infiltrated and the anatomy so distorted that the presacral nerve could not be found.

In a report that came out in 1927, Ferey (*Arch. Franco-Belge de Chir.* No. 8, 695, 1927) reported four cases of this procedure, two of which had been reported previously by him. Of the two cases previously reported one had been exceedingly successful and in the other pain had recurred. In the second two cases, the same thing happened. The patients apparently lived a sufficiently long time so that there had been regeneration of the presacral nerve.

I know little about the surgery of the pelvis but, I can imagine that in a certain percentage of these cases there would be a sufficient extension of the disease into the pelvis to make this procedure difficult. However, I think that this operation should certainly receive a trial based on the work done by different men. Certainly, in the hands of gynecologists, a presacral nerve resection would be a much easier procedure than a cordotomy. But there is the fact that out of the four cases reported by Ferey, there were two cases of recurrence.

With regard to trophic changes following cordotomy, they do occur particularly if there has been any tendency toward a trophic change before the operation was carried through. It must be remembered that many of these cases are very cachectic and if there is any breakdown of the skin prior to the operation that breakdown may become accelerated.

If cordotomy is properly performed and carried through by the technic which I suggest it is a very safe procedure in experienced hands. Dr. Smith's figures confirm this statement. We have had no difficulty of any kind in the last eighteen cases that have been done by this procedure, no motor difficulty, no retention for more than three days and no bed sores.

What do we mean by the relief of pain? We mean that patients do not require morphine and do not require any sedative or opiate to relieve their distress. A certain number of them are addicted to morphine before they come to us, so that it may be a week, ten days, or two weeks before the drug can be entirely withdrawn, but we do not consider any case as a success unless they are completely free of pain, requiring no more morphine after the operation has been performed.

**Complications of Radiation Treatment in Gynecology, Dr. Frank A. Pemberton, Boston, Mass. (See page 552, October issue.)**

#### DISCUSSION

DR. WILLIAM P. HEALY, NEW YORK CITY.—I would like to call attention to what we must expect to get from radiation therapy in the way of skin erythema doses in the rectal and bladder fields. We can visualize readily from observation of the skin on the abdomen what a single full erythema dose will do. As a rule it means desquamation changes in the skin. In the full four-field pelvic cycle which is used with the 200 kilo-volt machine, 15 by 15 cm. area on the skin, you get from  $1 \frac{1}{5}$  to  $1 \frac{1}{3}$  skin erythema doses in the bladder field. In the rectal field you get  $1 \frac{1}{3}$  skin erythema doses. You will sometimes see vaginal desquamation from a high voltage x-ray cycle alone without any radiation with radium whatsoever, and therefore you may see the same thing, possibly, in the bladder and rectum from x-ray radiation only.

It has been our experience in figuring out dosage that the bladder and the rectal fields in the treatment we use for cancer of the cervix will invariably get from

3 to 5 skin erythema doses, so we must expect changes to take place in those tissues as a result of this irradiation. It apparently is going to be quite out of the question for us to avoid damage to bladder and rectum with radiation therapy in treating cancer of the cervix.

A study of 50 cases of postradiation bladder complications at the Memorial Hospital shows about 2 per cent of bladder complications, primary, secondary, and tertiary. The primary occurred while the patient was receiving just the x-ray treatment alone and quickly subsided. The secondary resulted from desquamation in the bladder field, occurred in about three to six weeks after the radiation and disappeared sometimes without anything more than simple dysuria. The tertiary cases are those that usually fail to show symptoms of importance in less than one year after radiation has been given. They represent 49 of the 50 cases. There were four secondary cases, one of which cleared up and has never shown any other symptoms. The remaining 3 cases became tertiary later on.

Correct diagnosis is a most important point because further radiation may be fatal. Three of our patients had such severe hemorrhages that two of them died and the life of one was saved by doing a suprapubic cystostomy, packing the bladder, and giving three blood transfusions. We are unable to make a differential diagnosis between tumor and radiation ulcer without biopsy. None of the cases in this series gave any evidence on bimanual examination of tumefaction or fullness anterior to the cervical area.

As to the total amount of radiation that may cause the complications it has occurred in cases that received only 1000 millicurie hours of radium within the uterine cavity above the internal os, so apparently it can be a result of a very mild dose of radium.

As to the treatment of the disease, speaking only of the bladder cases, we found that they have to be treated when the symptoms are acute, with argyrol, when less acute with mercurochrome, but in the meantime the greatest relief is given by 1 per cent phosphoric acid bladder irrigations. One patient, a young woman thirty years of age, within six months after irradiation with radium and x-ray developed an acute lesion of the upper rectum and lower sigmoid. I did an exploratory celiotomy, having made a diagnosis of the lesions clinically, because of her rectal symptoms, and found that four inches of the rectum was apparently almost as gangrenous as an acutely suppurative appendix. It was swollen, red, mottled, rigid, hard, and apparently going to slough. She was a tap dancer and I felt that it would not be just to her to do a colostomy, so I placed the bowel down in the culdesac again, opened the posterior vaginal fornix, drained it above and below, and she made a perfect convalescence. It is now two years since I did that, and she is again working at her profession.

In another case Dr. Douglas Quick did a resection of the lower sigmoid two years after the patient had been treated with radium for cancer of the corpus. She had a fibrotic stenosis which caused complete obstruction, and she made a complete recovery.

DR. GEORGE GRAY WARD, New York City.—I have recently had the cases gone over at the Woman's Hospital to determine the cause and incidence of our complications. In the vast literature on radiotherapy there are comparatively few papers that deal specifically with a detailed analysis of complications in the different clinics. The prevailing opinion that exists, that the application of radium is an extremely simple process, and that anybody can do it is the cause, we believe, of a great deal of unnecessary suffering in the form of various complications. Regaud has stated very aptly that "it is necessary to have much experience to obtain from this method of treatment all the good that it may give without the evil that it may do."

An analysis of our material shows the following: In 558 cases of cancer of the cervix under my personal direction, there were 119 or 21.3 per cent that showed complications of some form or other varying from the minor to the severe type. In 106 cases of fundus carcinoma that we have had, 11.4 per cent developed complications. The mortality from radium therapy in all these cases was 1.1 per cent, with no mortality in Class I and Class II cases, limited to the cervix.

The types of complications: Nausea and vomiting during the application of the radium was not troublesome and was only sufficiently severe to be noted in 1 per cent of the cases. Cystitis and proctitis occurred in 4.5 per cent. Hemorrhage following the application of radium occurred in 10 per cent but there were very few of these cases that could be classed as severe hemorrhage or that required packing. Vesico- and rectovaginal fistulas occurred in 558 cases 22 times, or 4 per cent.

It was of particular interest to us to hear the reader of the paper bring out the fact that in cases that have had previous pelvic inflammatory disease, where the loops of the bowel may be adherent to the back of the uterus, there is undoubtedly considerable danger of rectovaginal or ileovaginal fistula occurring. This is in accord with our own experience. One remarkable case that I had was seen seven years ago with marked carcinoma of the cervix, Class III. She was radiated and there is no evidence of carcinoma today, although she developed a sigmoidovaginal fistula. It caused little trouble as it was small and unless the bowels were loose she did not bother about it and was able to do her work. Last autumn she developed severe pain over the sacrum, and we thought it was a bone metastasis but no evidence could be obtained of this by x-ray. Later an abscess developed which I opened and feces were discharged through the opening over the middle of the sacrum. X-ray studies showed that this connected with the original fistula via the sacrosciatic notch, which was sigmoidal and opened into the vagina. I made a temporary colostomy and sidetracked the fecal current and the patient has been apparently perfectly comfortable since. We hope that the fistula will heal, and we will then close the temporary colostomy. In cases where a supravaginal hysterectomy has been done and the stump of the cervix remains they are especially prone to damage to the bladder from irradiation and there is considerable danger of producing a fistula. In our series of 558 cases we had 40 cases which had had a previous supravaginal hysterectomy. In these cases hemorrhage occurred one and a half times more often, and fistulas were two and a half times more frequent. We are now careful to use a smaller dosage, repeated in these cases. Late obstruction of the ureter occurred in one-half of 1 per cent, and in the fundus cases we had no postradiation hemorrhages whatever.

DR. GUY L. HUNNER, BALTIMORE, MD.—There is nothing that disgusts me so much as the advertisements from the commercial radium concerns telling how to cure cancer with radium. If such results as reported today are obtained in the hands of the most careful men and in view of untoward results as I have seen following Dr. Burnam's use of radium, what can we expect from these men who know nothing about radium? It seems to me that our Society might consider that matter most seriously.

I have seen from 12 to 15 patients with very serious obstruction to the kidneys from the thickening in the broad ligament regions following radium treatment. Of course, no one can say how much thickening was there before the radium was used. We know how frequently in operating for cervical cancer we have to dig the ureters out of thick periureteral tissue, but these cases following radiation are among the most difficult cases of ureteral stricture that we have to deal with. They are very slow to give any degree of dilatation or of drainage but they do answer eventually and react very well to treatment.

**Pelvic Endometriosis and Tubal Fimbriae**, Dr. John A. Sampson, Albany, N. Y. (See page 497, October issue.)

**The Morphology of the Genital Epithelia, With Special Reference to Differentiation Anomalies**, Dr. Emil Novak, Baltimore, Md. (See page 635 this issue.)

#### DISCUSSION

DR. DEWITT B. CASLER, BALTIMORE, MD.—These growths are very much like carcinoma in their invasion and Dr. Sampson can trace them directly into the ovary itself. It is remarkable that these conditions have been missed up to the present time, and it is only due to Dr. Sampson's keen sense of observation that he has discovered them. I do not know whether the lesion is a common or a rare one but it probably was rare up to the present time because we have not been alert enough to find it, but I imagine that now if our attention is fixed more and more upon the fimbriated end of the tube, we will discover more of these lesions than we have heretofore.

If we can draw any clinical conclusions from these endometrial reactions, it seems to me that the one striking thing is this: We often see endometrial reactions in the incision following cesarean section. I do not believe we see them if the uterus is removed following cesarean section. We often see an endosalpingitis after a salpingectomy in the cornua of the uterus. We do not see them in the end of the tube, however, if a hysterectomy is done and the tubes are left in to conserve the blood supply, nor are we apt to see, so far as I have observed and so far as I know the literature, any reaction in the cervical stump following operation.

I believe that there must be some additional influence which has not yet been brought out. The uterus or possibly the tubes, but I believe the uterus, must exert some influence on these endometrial growths to cause them to grow in the way they do.

DR. RICHARD W. TELINDE, BALTIMORE, MD.—In spite of the many discussions in this Society regarding endometriosis, its etiology and its life cycle, the subject is not yet settled, although I believe that Dr. Sampson has quite definitely settled the etiology of this one particular type. No matter what theory one may propound to explain the etiology of endometriosis, there is some stumbling block in each case. For example, it is very difficult to explain such cases as adenomyoma of the extraperitoneal part of the round ligament on a pure implantation basis, unless we assume that there is also dissemination by the lymphatics. I believe the evidence for this is very scanty. Some years ago Sampson showed us endometrium near but not actually in a lymph gland and I have never been able to find endometrial tissue actually in a lymph gland in any case of endometriosis. There seems to be a very good evidence of implantation by means of surgical instruments in the case of endometriosis in abdominal scars. In many of these cases, however, there is actually a continuity between the endometrium of the uterus and that in the scar. I have seen, however, an implant in the lower end of the scar after hysterectomy in which no continuity at all could be traced between that implant and the cervical stump or the tubes.

From the clinical point of view one point has always impressed me and that is this: Regardless of how the endometrium gets into the ovary the dissemination throughout the peritoneal cavity by rupture of the endometrial cysts seems very probable. Sampson's recent work on carcinomatosis, in which he shows a similarity between the implants of carcinoma and endometrial implants, bears out this clinical impression.

There also is evidence that in some cases serosal metaplasia actually gives rise to endometrium-like epithelium. A few years ago Dr. Whitridge Williams demonstrated cases of decidual reaction on the posterior surface of pregnant uteri, indicating that the subserosal mesenchyme has, in the presence of pregnancy, become typical decidua. The epithelium lining the "glandlike" structures, which closely resemble the glands of pregnant uteri, could be traced as continuous with the serosa of the posterior surface of the uterus. This surely suggests serosal metaplasia in the case of this ectopic decidua. Furthermore I believe there is strong evidence against the implantation theory of this ectopic decidua because of the fact that this condition frequently occurs without any adhesions. Hofbauer described 15 cases of decidua on the posterior surface of the uterus occurring in 23 uteri in Williams' laboratory. He suggests that these might have a bearing on the etiology of endometriosis. A similar picture is found in the ovary at times in the presence of pregnancy in which case the continuity of the germinal epithelium with the glandlike structures can be traced. This again suggests the possibility of the germinal epithelium being the origin of the epithelium of the endometrial glands in ovarian endometriosis.

The evidence for dissemination of menstruating endometrium throughout the pelvis via the tubes has to my mind always been rather weak. Today, however, Dr. Sampson has shown us cases in which the tubal epithelium can be traced practically into the endometrial cyst of the ovary with a gradual transition between tubal epithelium and uterine-like epithelium within the cyst. That such a transition can occur between tubal epithelium and uterine epithelium, and vice versa, there is much evidence.

DR. FREDERICK J. TAUSSIG, St. Louis, Mo.—The history of medicine is full of controversies in which each man has bigotedly maintained a certain point of view and held to that point of view regardless of the evidence produced on the other side. I think we owe a debt of gratitude to Dr. Sampson and Dr. Novak for attacking this problem of endometriosis in a spirit not merely of defending a particular theory, but of arriving at the general truth. The concession that Dr. Novak made some years ago as to the implantation theory and the concession that Dr. Sampson made today regarding metaplasia from fimbriated portions of the tube are evidences of this spirit.

My experience with the question of implantation dates back to 1906 in connection with the study of a few cases of ectopic decidua formation. I looked up the literature on the peculiar distribution of these islands of ectopic decidua and, perhaps without real authority, suggested the possibility that detritus from the uterus passing out from the tube, implanted upon the pelvic peritoneum, was responsible in that way for the development of these decidual-like plaques.

As we look at the evidence that has been built up stone by stone, the whole subject is beginning to take form. Certain facts must be kept in mind. First of all, that the tubes are almost always open; next, that there is evidence of menstrual blood passing out through the tubes, and evidence of a peculiar distribution in the culdesac of tissue that can be only explained as implants; further, that there is, as Dr. Novak pointed out today, very definite evidence of the development of various forms of tubal, uterine, and even squamous epithelium from the celomic epithelium. Finally, there is evidence of traumatic metaplasia at certain points, as at tubal stumps and at the fimbriated ends of the tubes. I think with these facts in mind we cannot accept just one theory. First of all, we must agree that there occurs metaplasia in various portions of the genital tract without apparent cause. Secondly, there is definite evidence of implantation both in wounds and in the rupture of endometrial cysts, pointing toward the implantation theory. Third, there is the possibility of a certain activating substance passing from the tubal lumen out over the surface of the pelvic organs, and giving rise to the development

of islands of metaplasia. It seems to me that possibly this latter explanation may be more frequent than we have heretofore thought.

DR. CAREY CULBERTSON, CHICAGO, ILL.—I wish to speak on this topic chiefly from the point of view of the identification of the epithelial cells. We have given this matter a good deal of study in the histologic laboratory at the University of Chicago and feel that we have arrived at a place where the epithelial cells of the uterine gland can be differentiated from tubular epithelial cells. There has been some doubt occasionally expressed as to whether these hyperplastic growths, which we call endometrial in type, are merely that in appearance by low power or actually endometrium. A high power study of the epithelial cell of the gland shows certain characteristics which are for the present at least fairly definite. In the first place, the epithelial cell of the uterine gland is not granular during the ciliated phase, or at least the cytoplasm has very few granules, whereas the tubular cell is abundant in granules. That is fairly constant. However, the chief differentiation is that the uterine epithelial cell produces an abundance of glycogen and the tubular epithelial cell does not. These are points of differentiation that can be made. It does not follow, of course, that if it can be shown that in every case the epithelium of these apparent developments is not endometrial, that they may not be derived according to the theory that Dr. Sampson put forth in 1921. Some of these definitely menstruate. We have all seen sections of actively menstruating epithelial growths, always with stroma. Some of them were found during the stage when menstruation was absent and they are not menstruating. It is hard to say whether they would all be menstruating under certain phases.

In 1929 a study was made by Hartwell on the healing of wounds, illustrating the difference between the healing of subepithelial tissue and the epithelial cell, and he showed that the epithelial cell portion of the wound heals differently from that of the subepithelial tissue, in that the epithelial cells send out a substance so that there is practically a regeneration rather than a scar tissue formation; and that if this wound healing is modified, as it will be if it is subjected to inflammatory reaction, then we get hornification and not only duplication of cells but a tendency toward hyperplasia. It therefore seems that we can draw a direct analogy between that and the sections which Dr. Sampson has shown us, where there was a break between the tubal epithelium and those cells developing beyond.

DR. JAMES R. GOODALL, MONTREAL, CANADA.—It seems to me that Dr. Sampson's paper will cause us to change a great many of our beliefs. In the "spill" theory, to which most of us adhered, it was thought that the epithelium may be considered as a flower that carried with it its own soil. Today we have epithelium changing its character, but where does its soil come from? The interstitial cells of the uterus are unlike the glands. These are not present where the cells develop in situ by the method which Dr. Sampson has outlined, but they are always present in this type of endometriosis, and from what do they arise? We must assume that they arise locally therefore, and if that is the case, it would be a basal membrane or a basal cell which on one side develops into an epithelial cell and on the other into an interstitial cell.

DR. GRETE STOHR, NEW YORK CITY.—In his preceding paper Dr. Sampson has given a convincing interpretation of the genesis of certain forms of ectopic endometroid structures. The variety in localization of these structures and the variety of their morphology has advanced many attempts to explain this peculiar newgrowth on a uniform basis.

Among other theories, Halban, in Vienna, has explained endometriosis by a metastatic process, to which theory a case observed in the Woman's Hospital in New York seems to furnish further evidence.

A white woman, forty years of age, was operated upon for menorrhagia due to

a large myoma uteri on September 21, 1931; her last menstruation occurred August 31. A diagnostic curettage, limited to the cervical canal, was performed preceding supravaginal hysterectomy. The gross examination of myomas and myometrium did not reveal anything unusual, only the endometrium appeared slightly hyperplastic. A portion of the uterine wall was subjected to microscopic examination and a moderate glandular hyperplasia of the mucosa with mild basal hyperplasia was found, beside a few bare glands of endometrial type scattered in the adjacent muscle layer. In a group of large vessels, seated in the peripheral area of the vascular layer of myometrium, the lumen of one of them is found occupied by a fragment of glandular tissue which simulates in all detail uterine mucosa and which reveals also the identical type found in the endometrium. The tissue fragment lies almost free in the lumen, only at a short area it is adjacent to the vessel wall, without exhibiting direct contact with it. In an adjacent vessel a solitary fragmented gland of endometrial type without stroma coat is seen and in another section of the series a destroyed, frayed bit of tissue, in which distinctly a few cells in epithelial arrangement are distinguishable, is found lying free in a large lymph space.

Single endometroid glands or epithelial cells within the lumen of lymph vessels in the uterus were observed by Halban, Lahm and Davidofsky, in no instance however, does the literature reveal an incidence in which intravascular fragments of whole endometrium were encountered.

Whether in our case the preceding curettage may account for the separation and intravascular propagation, is questionable. There are pros and contras for this assumption which for the limited time cannot be discussed here.

I referred to this case in the form of a preliminary report. As a singular finding I do not consider it as the final link in favor of the metastatic theory, but I believe it is convincing enough to prove that the genesis of hysteroadenosis has to be sought in different biologic processes.

DR. SAMPSON (closing).—Dr. Casler asked about the frequency of primary fimbrial endometriosis. I do not know its incidence either in patients with or without pelvic endometriosis in other situations, because only recently have I been able to recognize it with any degree of accuracy.

The paintings of these lesions, which are reproduced in this paper, portray their appearance better than any verbal description. I have found it of great help to place the tube, after its removal, in a dish of normal salt solution in order to float out the fimbriae. Since primary fimbrial endometriosis develops most frequently in the terminal portion of the tubal mucosa of the fimbriae at or near the junction of the mucosa with the serosa of the tube, that of the mesosalpinx and the germinal epithelium of the ovary when the ovarian fimbriae extend to that organ, it is important to carefully inspect the bases of the fimbriae. I have encountered it most frequently at the bases of the fimbriae of the lateral surface of the tube.

I believe it is only one focus from which secondary pelvic endometriosis may arise by direct extension and dissemination, and even though it should prove to be a relatively infrequent focus it is of importance in the composite picture of pelvic endometriosis.

DR. NOVAK (closing).—Dr. Taussig, it seems to me, presented a judicious summing-up of the present status of opinion concerning the etiology of endometriosis. Dr. Sampson's new study, as presented today, indicates that even the histologic approach to the problem is not exhausted, as do also the observations embodied in my own paper. The former established the fact that at least a certain proportion of cases of ovarian endometriosis are produced by a direct metaplasia of tubal mucosa into endometrium, with invasion of the ovary as a sequel. This is in accord



with my own observations, which indicate further that the germinal epithelium itself is capable of such metaplastic transformation into either a tubal or uterine type of epithelium. It would seem that, as a result of such demonstrations as those reported here today, ovarian endometriosis is explainable without invoking the theory of implantation of regurgitated uterine mucosa, although I believe that Dr. Sampson still feels that the latter factor is probably the important one in a proportion of the cases.

There is still, too, a question as to the mechanism concerned in the production of the often widely scattered areas of ectopic endometrium in cases of pelvic endometriosis. Are these also evidences of metaplasia, or are they to be explained on the implantation basis? I do not know. As Dr. Taussig has said, the two viewpoints appear to be gradually converging, and it seems possible that before many years have passed Dr. Sampson and I might well be able to present a joint paper on the etiology of endometriosis.

### **Selection of Appropriate Operation for the Cure of Prolapse, Dr. Robert T. Frank, New York City. (See page 574, October issue.)**

#### **DISCUSSION**

DR. NATHAN SEARS, SYRACUSE, N. Y.—There has been a tendency recently to discredit the anatomy of the pelvic fascia as described by the anatomists, which is leading to considerable confusion among medical students. They are quite at a loss to understand the anatomy of the fascia around the vagina, the cervix, and the uterus. Personally I can see no more reason to doubt an orderly arrangement in the pelvic fascia than such an arrangement in the rest of the abdominal cavity or whatever part of the body may be studied. My own conception of the fascia is based upon surgical experience and dissection of four female pelves and briefly can be expressed as follows: Springing from and continuous with the superior levator fascia there is a double layer which rises into the pelvis; in the dorsal half of the pelvis it forms the uterosacral fold and in the ventral half of the pelvis it surrounds the cervix and the vagina.

DR. HAROLD O. JONES, CHICAGO, ILL.—At St. Luke's Hospital in Chicago, we have had a very definite attitude toward the pelvic tissues, including the uterus. We have felt that one of the indications for the selection of treatment was considerably influenced by the mortality of different procedures. Consequently, we have resorted to vaginal operations for the cure of these conditions. Of the cases operated upon by rather extensive operations for rectocele and cystocele, less than 300 Watkins' transposition operations, there was a mortality of 3. For cystocele and rectocele we have been satisfied with the type of procedure described by Dr. Frank and have had uniformly good success. The Watkins' transposition operation has been reserved for the very few cases that met the indications in this clinic, that is for the women past menopause who have rectocele. There has not been done in this institution a single suspension of the uterus for prolapse but they have all been satisfactorily treated by complete vaginal hysterectomy. The technic followed is that known as the Mayo procedure, with some modifications. After six of these cases where there was complete eversion of the vagina we had to completely obliterate this cavity. Three patients with complete prolapse had to have a subsequent operation. Two have urinary incontinence that occurred after imperfect repair of the anterior wall, and one had a LeFort operation after considerable descent of the vaginal vault.

DR. GEORGE GRAY WARD, NEW YORK CITY.—In my opinion, the operation of suspension of the uterus to the abdominal wall to cure prolapse is not suitable.

It is popular with some men doing general surgery but not with many gynecologists. It is better to approach the problem from below according to my experience. I use in the cases of elderly women both the transposition operation of Watkins and the Mayo operation. The Watkins' operation I limit to those cases where the prolapse is not extreme. If the cases are properly selected we get very good results from that procedure. In the cases where there is a definite prolapse of the cervix, protruding from the orifice of the vagina and associated with a large cystocele, I prefer to do a vaginal hysterectomy with a modified Mayo technic, as Dr. Frank has mentioned, and we have satisfactory results in a large proportion of these cases.

Where I have found failure in that operation is that while we always cure the cystocele, we sometimes have an enterocele develop when there is a deep culdesac of Douglas present. If it is not obliterated it may later cause trouble. Therefore, in all of my cases I utilize the procedure of removing the peritoneal culdesac and uniting the uterosacral ligaments with interrupted linen sutures, thus obliterating Douglas' pouch. Our failures with that procedure are very few.

DR. JOSEPH L. BAER, CHICAGO, ILL.—In 1928 it was my privilege to report on a series of 212 patients operated upon for prolapse at the Michael Reese Hospital. At that time I analyzed the results and will not repeat them but would say that 41 per cent of all the patients were operated upon by the transposition method. I had hoped one of the discussants would mention the Halban procedure, whereby the vesical peritoneum is pulled out into the vagina until its fixed point on the parietal peritoneum is reached. The fundus uteri is attached to that parietovesical angle in the abdominal wall from below. The essential prerequisite is that the over-all length of the uterus be shortened to three inches by cervical amputation, and finally the reconstruction of the pelvic floor is done. It is applicable to women in the childbearing period as well as to those in the menopausal years. We have had no recurrences.

DR. FRANK (closing).—Dr. Sears brought out a valuable point. I feel that dissections in the vicinity of the bladder are extremely misleading because any anatomist can bring out certain structures to the detriment of others. All one has to do to realize this is to read the various anatomies. Although I do not decry the study of anatomy, I feel from the point of view of the operator that these points which I have tried to emphasize are most essential.

Referring to Dr. Jones' remarks, I did not bring out the mortality but it is extremely low. In simple cystocele and rectocele with the cervix in its normal position, we still do the anterior and posterior operation with success. The interposition operation we have reserved for cases of large cystocele where the cervix is well up in position. In older women with large prolapse we do vaginal hysterectomy and obliterate the Douglas' culdesac if it is protruding, as it is in the majority of cases. If ventral fixation could be performed without the danger of incisional hernia and without additional risk, I would consider it the ideal operation in most cases unless a pendulous abdomen were present.

**Congenital Absence of the Vagina and Its Treatment, Dr. James C. Masson, Rochester, Minn. (See page 583, October issue.)**

#### DISCUSSION

DR. P. BROOKE BLAND, PHILADELPHIA, PA.—Next to determining definitely the true nature of faulty anatomical development of the genital tract, especially with regard to the determination of sex, there is no anomaly or type of maldevelopment more pathetic or more distressing psychologically than rudimentary growth, or still worse, a total absence of the canal itself.

Dr. Masson pointed out and stressed the rôle psychology plays in these unfortunate

patients. In considering operative therapy in general, it may be accepted, I think, as axiomatic that in most, if not nearly all, surgical conditions the decision as to when a patient should or should not be operated upon rests squarely on the shoulders of the surgeon. There are, perhaps, occasions when the proposition may be left to the patient to decide. This may be found, for example, in the disorder described by the essayist.

One can readily understand how a patient acutely conscious of a gross architectural defect in the organs fundamentally concerned with reproduction could very readily become a victim of neurologic imbalance, and, hence, for psychologic reasons, if for no others, interference may not only be instituted but at times it may become absolutely necessary.

With respect to interference in an operative way for an absence of the vaginal canal, wholly or in part, save for neurologic indications, I personally can see no advantage of adopting the recourse, unless the patient contemplates wedlock or is already married. Even in these circumstances it is questionable whether an artificially constructed vaginal canal is ever satisfactory anatomically. From the standpoint of restoration of physiology, one may look upon the measure without much optimism, or no optimism at all. As a copulative canal it may suffice, but rarely if ever does it serve in a reproductional capacity. When the vaginal canal is absent, nearly all observers agree, I believe, that the structures in the pelvis beyond are likewise absent or so dwarfed as to be utterly functionless.

In view of these convictions, it would seem that those cases of alleged offspring ensuing after the formation of an artificial vagina followed some operative measure not in gross, but in minor forms of maldevelopment, as, for instance, an imperforate hymen or a moderate type of atresia in an isolated area of the lowermost segment of the genital canal itself.

I have never seen an absence of the vaginal canal, complete or partial, without a total absence or an exceedingly rudimentary uterine body, as noted in the five patients studied and reported by Dr. Masson.

With reference to the type of operation to employ in the face of gross anomalous development of the vagina, I probably have been somewhat tardy as well as timid in resorting to major abdominal surgery. In caring for these patients I have followed rather consistently a conservative course. On two occasions the Schubert procedure was performed. The primary operative results were fairly satisfactory, overcoming in one patient a rather tormenting nervous state, and in the other there was established a canal suitable for marital purposes.

In the few other patients, probably four or five in all, reconstructive plastic flaps were used. In one patient of this group the operation was carried out because of contemplated marriage. This, following the operation, was consummated and the patient subsequently succeeded in raising three lusty children, by adoption!

DR. ROBERT T. FRANK, NEW YORK CITY.—Until Dr. Geist and I had devised a technic free of serious risk, I was always unwilling to attempt the construction of a vagina. The mortality incident to the Baldwin and Schubert technic certainly is greater than 10 per cent, and to my personal knowledge, a number of fatal cases have not been reported in the literature. In my opinion, it approaches 20 per cent. We are at present working on our fifth case in which the first tube flap was completely unsuccessful. In spite of this, the patient was never in jeopardy, and we are now completing the final stage with the flap taken from the opposite side of the thigh. Three results now date back to approximately five years and have proved permanent and satisfactory. Another vagina of two and one-half years' duration is likewise satisfactory. The mere fact that this procedure takes longer than the Baldwin or Schubert technic should not prevent the choice of this operation as its entire freedom from risk more than counterbalances this drawback.

**Intrauterine Radium Therapy as a Conservative Method of Treatment,**  
Dr. Walter T. Dannreuther, New York City. (By Invitation.)  
(See page 611, October issue.)

DISCUSSION

DR. ARTHUR H. CURTIS, CHICAGO, ILL.—Consideration must be given to the age which a patient should have attained before she is a fit subject for radium treatment of a malignant condition. I wonder whether we have not been making a mistake in accepting forty years as a satisfactory age limit? Should we not, as a routine, advance that age to at least forty-three or forty-four or even until the menopause is impending, rather than apply radium freely when the patient is as young as forty?

During rather recent times I have been confronted with a new pathologic entity, the occurrence of cancer in patients who during previous years have received radium as a therapeutic measure in nonmalignant conditions. I have personal knowledge of three of these patients; personal contact with two of them. The first came to me five years ago, at the menopause and bleeding. A diagnostic curettage was made and she was given approximately 2000 millicuries of radium within the uterine cavity. I examined the scrapings from the curettage and there was no suggestion of malignancy. Two weeks ago this patient returned to me with an incomplete obstruction of the cervical canal, with a little tarry discharge. I took her to the hospital, having no expectation that there would be serious trouble, and found an extensive adenocarcinoma of the body of the uterus. This patient may not have developed a cancer as the result of radiotherapy, but I suspect that this administration of 2000 millicuries was an indirect cause of its development because it caused obstruction of the cervical canal or that the cancer occurred as the result of endometrial irritation or a radium burn.

A second patient received a similar dosage, at the hands of another man, during her period of sexual activity, when she was about thirty. This was about twelve years ago. I saw her recently with an extensive carcinoma of the lower portion of the body of the uterus. A third patient was taken care of at Johns Hopkins Hospital in a similar manner.

DR. ROBERT T. FRANK, NEW YORK CITY.—I am glad of this opportunity to make a preliminary report of a new method of treatment which has been introduced by one of our dermatologists at the Mt. Sinai Hospital in the treatment of hemorrhagic diathesis.

The successful attempt of Peck and Sobotka to control experimental purpura in animals with moccasin venom led Peck to treat patient with hemorrhagic diathesis with this substance. He noticed that in women with thrombocytopenic purpura the tendency to prolonged menstrual flow was checked by means of the snake venom injections. This led him to treat uterine bleeding of various types with this therapeutic agent. In collaboration with Dr. M. A. Goldberger, 12 selected cases of uterine bleeding were treated. The majority of these patients had been treated over a period of months or years by means of curettage, transfusions, and other means without lessening the tendency to bleeding. A number of the patients had to be hospitalized because of a marked secondary anemia, the hemoglobin being below 35 per cent. Three were puberty bleedings, 7 were functional uterine bleedings, 1 was a metrorrhagia in a patient with a submucous fibroid, and 1 was prolonged and profuse menstrual periods in a case of Henoch-Schönlein's purpura. In all of the cases there was a marked therapeutic effect with a reduction in the duration and amount of bleeding. The majority of the patients were treated while they were

still bleeding and the control of the bleeding was seen as quickly as thirty-six hours after the first injection in a few of the cases. It usually, however, required from seven to ten days for a therapeutic effect to be noted. The patients have been under treatment from two to five months. In 3 of the patients injections have been discontinued but the length of time is too short for us to decide whether it will be necessary to resume the therapy.

**Method:** The venom used was that of the moccasin snake (*Ancistrodon piscivorus*). It was put up in 1:3000 dilution and injected intradermally. The initial injection was 0.2 c.c. and the subsequent injections were 0.4 to 0.5 of a c.c. given twice weekly.

The local reaction is unpleasant but not of sufficient gravity to prevent the patients from returning for new treatments every five days.

**DR. GEORGE GRAY WARD, NEW YORK CITY.**—I wish to report an experience similar to Dr. Curtis'. A patient came to me some seven years ago, about at the time of menopause, having a uterus which was evidently enlarged, symmetrical, and with menorrhagia. It was a case selected for radiotherapy. She had the usual dosage of about 1500 milligram hours. This patient was perfectly well for seven years. She came into the follow-up clinic the other day with slight bleeding and a diagnostic curettage showed adenocarcinoma. The original pathologic findings at curettage were negative.

Another case of interest in this connection was that of a colored woman twenty years old who had never been pregnant, who had a fibroid of the uterus and excessive bleeding. Hemoglobin 15 per cent, 720,000 reds. She was given two transfusions and radium was used, 2000 milligram hours. She had complete amenorrhea for five months. She came in several months later pregnant and delivered a perfectly normal healthy boy.

**The Treatment of Gonococcal Infections by Artificial (General) Hyperthermia, Drs. Stafford L. Warren, and Karl M. Wilson, N. Y. (See page 592, October issue.)**

#### DISCUSSION

**DR. C. FREDERICK FLUHMAN, SAN FRANCISCO, CAL.**—I should like to draw attention to another method of producing hyperthermia, namely by the use of hot baths. This procedure was mentioned by the ancient Egyptians, Greeks, and Romans, but it is only within the past few years that it has been done while checked with a thermometer. Schamberg employed baths for sterilizing chancres and the method was further developed by Mehrten and Pouppirt for the treatment of neurosyphilis. Dr. A. V. Pettit, one of my confrères at Stanford, conceived the idea of using it to treat gonorrhea and this study has now been conducted by him for a period of over two years. The patient is immersed in a hot bath, the temperature of the water being about 105° and gradually increased. The patient's temperature is taken every five minutes, and it can be raised to 104° or higher within a half hour. She is kept in the bath for a period of one hour, and one bath is given daily for four consecutive days. This, of course, is a hospital procedure, and each patient has a very careful preliminary examination, while an interne sits by the bath and watches her during the whole course of the treatment. Of 62 patients who have been treated to date, representing all types of inflammatory conditions of the pelvis, 38 are cured, 11 improved, 3 show no improvement, and 10 have had no follow-up. The criteria for a cure is that the patient must be well within three months, must show repeated negative smears, and have no demonstrable pathology in the pelvis.

Of considerable interest is the fact that the deep lesions are the ones apparently most readily influenced, while the superficial are most resistant. In preparation for the treatment the vagina should be scrubbed thoroughly with soap and water because if this is not done the patient may reinfect herself immediately afterwards since gonococci present in her vagina may survive. It would seem, therefore, that it is not only the effect of the high temperature on the gonococci which produces these good results, but some other factor which is induced by the hyperthermia.

DR. PHILLIP F. WILLIAMS, PHILADELPHIA, PA.—I would like to ask about the clinical applicability of this method of treatment, particularly in regard to two types of cases, gonococcal infections in pregnant women and in young children. In the majority of instances when a pregnant woman develops a febrile infection of high degree it frequently terminates the pregnancy. I should like to have Dr. Wilson's opinion as to whether pregnant women should be subjected to this method of treatment? One of the most difficult problems we have in the gynecology of childhood is the treatment of cervicitis, commonly called vaginitis, of young children and I would like to know whether Dr. Wilson feels that the extreme degree of hyperthermia that he has used would be advisable in the treatment of infants and young children?

DR. WILSON (closing).—We have not had enough experience with this method to be too specific about the results obtained. I did not have an opportunity to mention that in this series I presented one patient who had a lower birth canal infection, unknown to us, was pregnant at the time we treated her. She missed her following period and at the present time is approaching term without any damage. I do not recommend it as a therapy to carry out on a pregnant woman for I think it might be disastrous. One of those women reported we followed for over a year. She has since been pregnant and was delivered spontaneously and showed no trouble of any kind in the puerperium. This seems to me a good test of the permanence and efficiency of the cure. If we get a series of negative bacteriologic results and then a patient comes back with positive smears, one can never be sure that it is not a reinfection. We have had several examples of that.

We do not recommend this form of therapy as a routine treatment for gonorrheal infections at the present time. The technic must be much improved, but we do want to emphasize the principle of therapy, and that the usual strains of gonococci can be killed in the body on exposure to a temperature which can be tolerated by the patient, for a specific length of time. We are changing this technic already and during the last month or two we have a series of patients not included in this paper, and which have not been observed for a sufficient length of time to draw any conclusions, upon whom we have carried out the same principle of therapy but without any diathermy apparatus at all, using only radiant heat. It takes a little longer but the results are going to be equally satisfactory apparently and there is no danger of burning the patient. Several of our patients in this series did have small superficial burns at the point of contact with the electrodes.

I believe the ultimate technic will probably be a combination of local and general heat. One can raise the temperature to the desired level by local methods but it is so quickly dissipated by the blood stream that it will not be maintained for the requisite length of time to kill the organisms. If one elevates the body temperature to a somewhat lower level than we have shown here, say 40°, and supplements that by local heat at a higher level, it would be much easier for the patient and I believe the results will be equally satisfactory. It is the principle involved in the therapy, as I said, rather than the technic that I want to emphasize.

**The Diagnostic Value of Radiopaque Contrast Media in Gynecology and Obstetrics,** Drs. Alexander M. Campbell, J. Duane Miller, Thomas O. Menees, and L. E. Holly, Grand Rapids, Mich. (See page 542, October issue.)

#### DISCUSSION

DR. ARTHUR H. CURTIS, CHICAGO, ILL.—We must beware of the too frequent employment of lipiodol. There is considerable danger of producing at least a mild inflammatory intraperitoneal reaction. I have seen several patients treated with lipiodol elsewhere, in whom there was a marked inflammatory reaction. I therefore warned that we must not use lipiodol in cases other than those in which it is urgently necessary, such as preliminary to surgical work for relief of sterility. Lipiodol is of undoubted diagnostic value, but it must be used with caution.

DR. ROBERT T. FRANK, NEW YORK CITY.—I can only say that I am heartily in accord with what Dr. Curtis has stated. We have seen one pelvic abscess follow lipiodol injection. In another case in which it was necessary to open the abdomen a chronic peritonitis was found (due to encysted lipiodol) which involved the ovarian region. I believe lipiodol is harmful in cases of sterility. In consequence of such findings at my own clinic I have limited the use of lipiodol to cases where the tubes have previously been proved closed by air insufflation.

DR. CAMPBELL (closing).—When this paper is read it will be found to have covered all the criticisms mentioned. We brought out carefully the technic that should be employed and accentuated the care that should be taken in selection of cases. We do not believe that the use of lipiodol is any more harmful than any other diagnostic gynecologic procedure if it is carefully done in selected cases and in cooperation with a competent radiologist. We feel, however, that we must sound a note of warning against the indiscriminate use of uterosalpingography in the hands of those who neither understand its technic nor its contraindications. The same comment should apply to the use of amniography.

*(To be continued in December issue)*

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### NEW YORK OBSTETRICAL SOCIETY

*MEETING OF JANUARY, 12, 1932*

DR. E. EVERETT BUNZEL reported **A Case of Marked Hydramnios in the Fifth Month of Pregnancy.** (For original article see page 755.)

#### DISCUSSION

DR. G. H. RYDER.—Personally, I do not remember ever seeing marked hydramnios except with multiple pregnancy or abnormality of the fetus.

In the first 20,000 deliveries in the old Sloane Hospital, there were recorded 113 cases of marked hydramnios, an incidence of 1 in 177. Of these 20 were with twin pregnancies, 3 with triplets, and 5 with monstrosities. So that of the total 113 cases of hydramnios, 28, or 25 per cent were associated with multiple pregnancies or monstrosities.

In the whole series of 20,000 deliveries, there were recorded 244 sets of twins and 4 sets of triplets. Therefore, 8 per cent or 1 in 12 of all twin pregnancies, and 75 per cent or 3 out of 4 of all triplet pregnancies, showed marked hydramnios.

Of the 113 cases of hydramnios, 81 were in multiparae and 32 in primiparae. There were 62 abnormal presentations, and albumin was present in 65 or over half. Labor was premature in 49 and near term in 64.

There was no maternal mortality, but the fetal mortality was high. Of the 141 infants born, including multiple births, 65 were lost, or 46 per cent.

During the last year in private practice, I have had 3 cases of marked hydramnios. Two were in twin pregnancies and one was associated with a fetal monstrosity. Both twin pregnancies terminated spontaneously near the seventh month, 3 of the 4 infants dying of prematurity.

The case associated with fetal monstrosity is worthy of mention. A young primigravida, after slight nausea in early pregnancy and an attack of acute catarrhal jaundice in the fifth month, was seemingly normal until eight weeks from term, when she suddenly became greatly distended with liquor amnii. Her abdomen suddenly became the size of that of a woman at term. Severe Braxton-Hicks contractions precluded sleep. The cervix was well thinned out, one and a half fingers' dilated, with bulging membranes. Labor seemed imminent. But a two weeks' rest in bed with hypnotics and restriction of salt from the diet, caused abatement of all symptoms. The contractions ceased, the size of the abdomen diminished to that of a normal seven and a half months' pregnancy, and the cervix contracted down and closed. A week later, five weeks before expected confinement, labor started. This seemed normal, except that the uterus was asymmetrical, bulging out alarmingly on one side as though it might rupture. Full dilatation of the cervix soon occurred and the small fetal head was easily lifted out with forceps, but the correspondingly small body could not be delivered. After much difficulty, this was accomplished, and the cause of the trouble was seen to be an enormously distended fetal abdomen, the size of a football. The superficial veins around the navel were much distended. The child made only one or two feeble attempts at breathing. Autopsy showed a large dermoid cyst, adherent to the surrounding tissues and compressing the heart and lungs up into the thorax. The remaining fetal organs were normal, except that the ovaries were absent.

The most marked case of hydramnios that I have ever seen, occurred while I was resident at the Sloane Maternity Hospital. A country doctor telephoned that he had a pregnant woman with a "terrible malady." On admittance to the hospital, the patient presented a never to be forgotten picture. Her face was haggard and jaundiced, her abdomen was distended enormously, so that when she lay on her side with legs flexed, the dome of her abdomen extended as far out as her knees. The abdomen was so tense that the gentlest tap with the finger caused pain. Vaginal examination showed the cervix well thinned out and dilated 3 fingers, with tense bulging membranes. These were punctured and the cervix easily stretched to full dilatation. A small fetal back presented. A foot was grasped and a healthy fetus was easily delivered by the breech. A second sac of bulging membranes was found with a second fetus lying transversely. This also was delivered by the breech. The doctor guarding the fundus remarked that there was a third fetus. This also was delivered by the breech. Three healthy children were now kicking on an adjoining table, while three navel cords were hanging out of the mother's vagina, a most unusual sight. The two placentae were extracted manually and the uterus was packed with 5 per cent iodoform gauze, to prevent relaxation and hemorrhage. The three babies weighed together  $17\frac{1}{2}$  pounds. With the placentae and the enormous amount of liquor amnii this woman had been carrying a really tremendous weight. The mother made an uneventful recovery and all three children grew to adult life.

DR. R. M. BEACH.—I had practically the exact counterpart of the last case a number of years ago. The patient was about five months' pregnant, and I had the opportunity of observing her for three or four days. The abdomen increased an inch a day. The interesting symptom in her case was a very rapid pulse, from 130 to



140. She had three distinct syncopal attacks on the street due to this rapidly developing acute hydramnios. We took her to the hospital and ruptured the membranes, but, unfortunately, she would not go into labor. We waited four or five days and then did a vaginal hysterotomy, delivering a pair of twins. She made a very good recovery.

DR. RAPHAEL KURZROK, by invitation, read a paper entitled **Biochemical Studies of Human Semen—Factors Affecting the Migration of Sperm Through the Cervix.** (For original article, see page 19, April, 1932, issue.)

#### DISCUSSION

PROF. EDGAR G. MILLER, JR.—Dr. Kurzrok has very properly stressed the view that there must be some orienting mechanism which starts the migration of the sperm from the vaginal culdesac toward its destination in the fallopian tube. The mere random swimming would seem to be inadequate. It is possible that the orgasmic reactions of the uterine muscle may in certain cases aid in the movement of sperm into the uterus, but conception can occur without this mechanism. The phenomenon described by Dr. Kurzrok offers a possible factor in the preliminary orientation of the sperm migration on purely physicochemical grounds.

The mucus plug in the os would seem to offer a physical barrier to the migration. However, its alkalinity favors sperm motility, and, once entered, the sperm are quite able to swim in it. On the basis of the work reported, the mucus appears to have a positive function in the orientation, and the maintenance of its normal alkalinity seems to be a matter of some importance in this function. Because of its high alkalinity ( $P_H$  9.5) it has a very much greater concentration of hydroxyl ion, and less of hydrogen ion, than the slightly alkaline semen in contact with it ( $P_H$  7.8); there is an even greater gradient of concentration of these ions at the interphase between the semen and the vaginal wall ( $P_H$  3.6). Where these fluids, of different degrees of alkalinity or acidity, are in contact, there is naturally a tendency for the ions to diffuse to establish equal concentrations. The hydrogen ion, with its positive charge travels perhaps five times as fast as the average associated anion (negative), while the hydroxyl ion, with its negative charge, travels perhaps four times as fast as the average cation (positive). Consequently, there is a separation of positive and negative charges, the mucus becoming more positive because of the hydroxyls leaving it faster than the positive ions do, while the positive hydrogen ions are coming in from the semen ahead of their anions; in the semen at the contact boundary the reverse is occurring. This builds up a difference of "electrical pressure." A potential difference must occur in vivo at this phase boundary. Probably the "diffusion potential" described is the most important factor; there are also other factors which make it certain that a difference must occur. In vivo conditions cannot be exactly duplicated in vitro. The potential differences measured (3-5 m.v.) were obtained in vitro. I believe that they may be greater in vivo. Three to 5 m.v. may not seem to be a very great figure; but when applied over a distance of, at most, probably 50 micra, it becomes a respectable gradient. And this gradient, as Dr. Kurzrok has reported, will apparently cause a movement of the negatively charged sperm toward the positive side of the gradient. This movement seemed to be a cataphoresis. It is perhaps surprising, in view of results obtained by other workers on sperm of lower animals, that galvanotropism was not observed.

I believe that, apart from the special application of this in the physiology of the sperm in the tract, the most interesting point is that it offers a hypothesis to explain how a so-called "chemotaxis" may occur.

Dr. Kurzrok has, I believe, presented a reasoning by analogy from in vitro experiments that applies logically in the body. He has described what is probably one,

and perhaps not the most important, factor in a rather complex and largely unknown mechanism which determines the path of the sperm migration.

In reply to Dr. Moench's questions, the value of  $P_H$  9.5 for the mucus is taken from other publications on the subject. Perhaps it is too high. However, the potentials reported were measured on normal material, and not calculated from theory. Moreover, acidification of the mucus destroyed the potential differences and pathologic, less alkaline mucus samples gave a similar reduction or even reversal. The voltage gradient seems to depend on the  $P_H$  gradient.

As to the question about thigmotaxis of sperm for oil droplets and other "inert" masses, no explanation is attempted. One suspects that surface tension phenomena are frequently involved. How far electrical forces may be called in explanation I do not know. The phenomenon described by Dr. Kurzrok seems, in our experience, to be unique for alkaline mucus.

DR. G. L. MOENCH.—In the marine animals there is a jelly which surrounds the ovum and the function of this seems to be to hold the sperm. I have often wondered whether the cervical mucus did not have a similar function.

I have not any apparatus to measure the potentials, but I took the cervical mucus and put it on a glass slide and found very much the same thing, namely that the sperm gathered at the junction of the mucus and the semen. I wondered whether that was simply due to the difference in viscosity and tried mineral oil and found they did exactly the same thing with the mineral oil as with the mucus; they gathered in a thick row at the border, and it seemed to me that at some point there was a physical break, but suddenly one would get through—the mineral oil not being a very good preservative—and after a while they got to wiggling and died. I then greatly increased the thickness by trying some of the various contraceptives on the market and found in those contraceptives where there was not any actual poison for the spermatozoa, they finally penetrated.

After referring to the penetrating qualities of the sperm and the mechanism of such penetration, Dr. Moench went on to say that he found the  $P_H$  of the cervix is lower than 9.5. I am not trying to contradict the biochemists at all, but I have taken it at the outside of the cervix where it is in contact with the vaginal  $P_H$ , and further up it is a little higher, so, after all apparently the  $P_H$  is between 9.5 and 3.5. I was able in one case to get a  $P_H$  in the vagina of less than 1.8. The potential of lactic acid being something like 0.5 and 0.8 that reduces the electrical charge very much. I do not think it influences the mechanism of the thing.

DR. W. H. CARY.—I have made a study of the behavior of sperm cells in the female secretions over a period of many years. Careful, postcoital, biologic investigations have been completed in well over 300 childless marriages. These observations indicate that sperm cells promptly and vigorously invade the inviting alkaline medium offered by the cervical secretion and that sperm migration is adversely influenced in direct proportion to the increased viscosity of this medium. The prompt occurrence of pregnancy in patients long sterile following some simple item of treatment, such as douching, the application of suppositories or tampons, or the passage of a sound, has doubtless taken place in the practice of many present and is to be ascribed to the correction of mild degrees of hyperviscosity. The large number of women who become pregnant in spite of habitual and prompt contraceptive douches would seem to indicate that the electrical influence which Dr. Kurzrok describes at the point of contact between the seminal pool and cervical secretions is most essential, at least, to sperm migration. These douches must either wash away the seminal pool or seriously alter its chemical character, and yet failure of contraception by douching is reported in as high as 33 per cent of these patients. Added experience has made me increasingly humble in attempting to explain the manifold influences during sperm migration. I feel certain, however, that the hazard which the viscosity of the cervical secretion normally exerts against migration of the sperm cells screens out weak and abnormal

cells from the invading host and that nature thus carries out its great principle of natural selection.

DR. KURZROK (closing).—The measurements of hydrogen ion vary quite markedly according to the type of apparatus used, whether it be a colorimeter or a glass electrode. Some of our experiments were carried out with a glass electrode while others were done with a colorimeter. The vaginal acidity is not a perfectly fixed thing. I believe that there are certain variations in it, depending probably upon the function of the ovary. What we want to stress is the fact that there is a potential gradient upward into the cervix and uterine cavity. As Dr. Miller said, we can not in any way duplicate in vitro the exact conditions that are present in vivo. We can only make relatively normal conditions.

In reference to the point raised by Dr. Cary as to how spermatozoa will manage to get up the cervix after a douche, I want to remind him first of all that a great many sperms may mechanically stick to the cervical plug of mucus. Many douches have a precipitating action on proteins and I can think for the moment of a possible precipitation of the surface of the mucus just beyond the point where the sperms have reached and what you have done there really is to seal off the sperm against further action of the douche. That is a possible explanation.

We have not solved this problem of migration: we have merely indicated a possible way. It is reasonable; it follows sound physiology, biology, and biochemistry. We have not explained the whole thing by any means. We have been trying to evolve some mechanism that may help us to understand the migration of sperm and in this way help us in some of the problems of sterility.

DR. ISIDOR C. RUBIN read a paper on the **Diagnosis of Peritubal Adhesions and Tubal Strictures by Uterotubal Insufflation.** (For original paper see page 729.)

#### DISCUSSION

DR. ROBERT L. DICKINSON.—May I ask if it is a fair inference that removal of the isthmus and reimplantation of a tube, as is done for some sterilities, will not so cripple the rhythmic contractions in the tube as possibly to make such an operation useless? There are thirty different operations of that kind and some of the most popular consist in sticking the shortened tube into the uterus and leaving the tube patent and supposing that a half a tube that is patent is nearly as good as a whole tube.

DR. W. H. CARY.—I desire to mention two points of possible interest to gynecologists who carry out patency tests without kymograph tracing. With proper apparatus and sufficient experience the physician should be able to make the patient entirely comfortable when ready to release the gas column, and the pressure should be raised so slowly that the operator may take cognizance of any subjective complaints by the patient and carefully record the location of pain and the gas pressure at which it occurs. The patient should be previously instructed to promptly report the site of any new pain during the test. Adhesions or obstructions at the outer portion of the tubes frequently reveal themselves by lateral pelvic pain at a gas pressure of approximately 120 mm. or more. Intramural occlusion does not commonly give this result. Secondly, bimanual examination should immediately follow the termination of insufflation. In certain abnormal cases a distended tube may be palpated. A primary drop in gas pressure may be due, one must remember, to the relaxation of intramural spasm even though the fimbria be closed.

DR. RUBIN (closing).—Dr. Dickinson is quite right. If one were to judge from that one case the operation is practically useless. It served the purpose of demonstrating what the ampullary portion of the tube will do, and that brings up a ques-

tion, namely, what one can accomplish by operation. This is not the time, however, to discuss this point.

Dr. Cary's suggestion is a very practical one. I have been able to locate the point of blockade by clinical tubal insufflation in practically all cases, which checked with the lipiodol examination.

In regard to the pressure at which pain is elicited, I find it varies but as a rule it takes more than 100 mm. of mercury to cause pain. It continues as long as the gas pressure is maintained, particularly if it rises to higher levels, and then it takes 30 or 40 mm. of drop to cause its disappearance.

A practical suggestion is in order. When a kymograph is not at hand it would be possible to plot out the curve described by the pressure fluctuations by watching the behavior of the mercurial column in the manometer. Of course, it is not as exact as the kymograph because the kymograph gives pressures in terms of time. The kymograph, after all, is an instrument of precision, and if one wants to arrive at accurate diagnosis of constrictions and tubal strictures, this instrument is indispensable.

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## CHICAGO GYNECOLOGICAL SOCIETY

STATED MEETING, JANUARY 15, 1932

DR. HARRY O. MARYAN described **An Electrical Device for Grinding Tissue Under Aseptic Conditions.**

DR. J. P. GREENHILL presented a specimen of **Adenocarcinoma of the Ovary Associated With Pregnancy.**

This woman, a tertipara, aged thirty-three years, was admitted to the Cook County Hospital complaining of pain and a swelling in the abdomen, loss of weight and amenorrhea of three months' standing. During the past three years she had had various periods of amenorrhea. General examination was negative except for a slightly enlarged thyroid. The basal metabolic rate was plus 13. The abdomen was markedly distended. Two large masses could easily be felt. No fetal heart tones could be heard. On vaginal examination three large masses were easily outlined. One mass filled the culdesac, a second one felt like a three months pregnant uterus and on the right side was another very large, soft, cystic mass. The diagnosis made was pregnancy complicated by an ovarian tumor. X-ray examination proved to be negative for pregnancy.

At operation there was found a three and one-half months' pregnancy associated with a large ovarian tumor which measured approximately 20 by 15 by 15 cm. One-half of the tumor was solid and proved to be a papillary adenocarcinoma. The other half was a simple serous cyst. All over the abdomen as high up as the left kidney region there were metastatic nodules. The pregnant uterus, the tumor and the left ovary were removed. The case is reported because of a similar one presented by Dr. Danforth at the December meeting.

DR. M. A. SCHNITKER (by invitation) and DR. F. E. WHITACRE presented a paper entitled **X-Ray Diagnosis and Fetal Death.** (Published in the *American Journal of Roentgenology*, September, 1932.)

DR. JOSEPH B. DE LEE presented a motion picture demonstrating the **Treatment of Breech Presentations.**

DRS. CORNELL and WARFIELD presented a **Preliminary Report on the Use of Skiodan for Visualizing the Urinary Tract During Pregnancy.** (Published in this JOURNAL, May, 1932, page 755.)

# Department of Reviews and Abstracts

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CONDUCTED BY HUGO EHRENFEST, M.D., ASSOCIATE EDITOR

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## Selected Abstracts

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### Carcinoma

**Bonney, V.:** Surgical Treatment of Carcinoma of the Cervix. *Lancet* 218: 227, 1930.

The author encourages the use of the Wertheim operation, since his results with it are better than with radiation. His only exception is the inoperable group.

Radiation is not used in conjunction with operation but reserved for the inoperable cases.

In his series of 284 operations, 110 patients were well at the end of five years, while in 181, 55 were well at the end of ten years. The rate of cures is considerably changed when considered on the basis of glandular involvement: in 160 without involvement 81 were well, while in 124 with involvement only 29 were well after five years.

In 382 patients, 55 deaths occurred, 25 from shock and 15 from sepsis. Once the operation was completed in 27 minutes but speed is less of an objective. From his first 100 to his last 98 operations the operative mortality rate was lowered from 20 to 8 per cent.

About 68 per cent of the recurrences occurred within the first two years.

The writer feels that the true worth of this operation cannot be judged until it has been tried in other countries. This also applies to radiation therapy.

H. C. HESSELTINE.

**Philipp, E.:** Statistics on Carcinoma of the Cervix Uteri and of the Vagina of the Years 1923-1925. *Zentralbl. f. Gynäk.* 56: 212, 1932.

Statistics of 484 cases of carcinoma of the cervix and 15 cases of carcinoma of the vagina observed from 1923 to 1925 in Professor Stoeckel's clinic in Berlin are presented. The cases arranged themselves as follows: operable, 183 (40.8 per cent); borderline, 85 (19 per cent); inoperable, 180 (40.2 per cent).

Of this number, two of the inoperable cases were moribund on admission and died before treatment could be instituted. Of the remaining 446 cases 161, or 36 per cent, are well and free from recurrence. Classifying these cures according to the group into which they were placed at initial examination, it was found that: of the 183 operable cases, 105 or 57.3 per cent; of the 85 borderline cases, 27 or 31.7 per cent, and of the 178 inoperable cases, 29 or 16 per cent are well without recurrence.

Comparison between cases submitted to Wertheim operation, and those submitted to radiation gave the following results.

	OPERATION (131 CASES)		RADIATION (315 CASES)	
	NUMBER TREATED	PER CENT WELL	NUMBER TREATED	PER CENT WELL
operable	109	62.0	74	50.0
borderline	19	31.5	66	32.0
inoperable	3	0.0	175	16.6

Those cases treated by radiation gave an absolute percentage of healing as follows: 255 cases treated with radium alone, 74 (29.1 per cent), and 60 cases treated with radium and x-ray, 13 (21.7 per cent) are well without recurrence.

There were 15 cases of carcinoma of the vagina of which 3 were operable, 1 was borderline, and 11 were inoperable. One case from each group is well without recurrence, and all of these three cases were treated with radium.

WILLIAM F. MENGERT.

**Begoin: Cancer of the Cervix and Hysterectomy. Ten to Twenty-five Year Results.** *Bordeaux Chirurgical* 9: 1, 1930.

The author performed 75 radical Wertheim hysterectomies between 1904 and 1918. There were 6 operative deaths. Follow-up data were obtained on 40. Of these 20 are dead. Of the 20 still living and well, more than 20 years have elapsed since the operation in 5, more than 15 years in 5, more than 12 years in 5, and more than 10 years in 5 cases.

In reviewing the literature, the author has been unable to find many reports of statistics where the patients had been followed longer than 10 years. He was, however, able to collect 1,881 cases among which there were 7 instances of recurrence between 5 and 10 years after operation, while at the end of the 5 year period the patient had been apparently well. From this he concludes that although recurrence after 5 years may occur, it is comparatively rare and a 5 year cure may be considered as a complete cure.

THEO. W. ADAMS.

**Weibel, W.: The Operative Treatment of Carcinoma of the Female Generative System.** *Med. Klin.* 26: 117, 1930.

Among 2,000 cases of cancer at the Prag woman's clinic the distribution was as follows: Cervix of the uterus 80 per cent, body of the uterus 5.5 per cent, ovary 8 per cent, vulva 2 per cent, vagina 4 per cent and tube 0.25 per cent. The least malignant is cancer of the corpus uteri and the most malignant are cervical and ovarian carcinomas.

Operation should be radical in all cases except for cancer of the body of the uterus. In these cases a simple vaginal total extirpation is sufficient because the parametria are practically never infiltrated. The operative mortality is low and the percentage of cure high.

On the other hand, the operative mortality for cervical cancer is high and here also the vaginal approach is safer than the abdominal. The percentage of five year cures is not very high because a large proportion of the patients already have lymph gland metastases at the time of operation.

Weibel advises the vaginal operation for old and debilitated patients, for those with bad hearts and lungs and for early cases. For the advanced cases with parametrial and gland involvement, it is preferable to perform the radical abdominal operation.

For cancer of the vagina, an abdominal radical operation should be done. However, operability is low and permanent cures are few in number. For cancer of the vulva, an extensive operation must be performed.

In cases of ovarian carcinoma the operation should be radical and should be followed by radiation.

Cancer of the tubes has a most unfavorable prognosis for the chance of cure is only 4 per cent.

Every radical or palliative operation should be followed by roentgen ray treatment over a period of six to twelve months because there is no doubt whatever that postoperative irradiation in cancer of the female genitalia improves the chance of recovery.

J. P. GREENHILL.

**Kamniker: The Improvement of Results in the Treatment of Uterine Carcinoma.** Wien. Klin. Wchnschr. 43: 943, 1930.

At the Peham clinic it has been found that the best results in the treatment of the uterine carcinoma are obtained by utilizing operation by the vaginal route, post-operative radium and x-ray therapy. There is a difference of 16 per cent in cures between those who have had and those who have not had postoperative radiotherapy. Considering this highly specialized form of treatment, the author strongly advises the physician to refer patients with uterine carcinomas to clinics where the treatment is available, in the hope that this will greatly improve the results obtained.

FRANK SPIELMAN.

**Voltz: Physical Therapy in Gynecology.** Therapie der Gegenwart 72: 29, 1931.

The author reports the results of radiation therapy at the Doederlein clinic. In all 1319 patients suffering from carcinoma of the cervix were treated by radiation during the years 1913-1923. Of these 225 or 15.4 per cent resulted in absolute five year cures. These figures include all cases treated at the clinic, even those classified as advanced, hopeless or moribund on admission. During 1923-1925, 171 additional patients were treated by radiation and 40 of these, or 23.3 per cent resulted in absolute cures. This marked increase, the author feels, is due to improvements and refinements in technic. Of the Group I cases 41 per cent resulted in absolute cures as compared with 23 per cent cures in Group II. Group III showed 11 per cent absolute cures and even in Group IV there were 9 absolute cures. It is in these latter Groups III (the inoperable) and IV (the hopeless) that the results obtained, though small, are striking for without radiation therapy, all of the patients in these two groups were doomed.

The results in corpus carcinoma were also striking. Of all patients with carcinoma of the corpus uteri 41 per cent were permanently cured. Of the operable cases 66 per cent resulted in absolute cures; 10 per cent of those patients showing residual growth following surgery were also cured. Vaginal carcinoma gave a 5 per cent and vulvar carcinoma a 12 per cent cure.

These figures compare favorably with those in the literature of the world which show 17.4 per cent cures for all cases and 42.7 per cent cures for cases in Groups I and II. The absolute cures for corpus carcinoma in the literature is 35.6 per cent for all types and 56.5 for the operable group.

Radiation therapy also gives excellent results in the treatment of menorrhagia and metropathy. Here the operative mortality is still 5 per cent whereas Gauss has reported 5,000 consecutive patients treated by radiation therapy with only 5 deaths. The results furthermore were excellent, 95 per cent of patients with climacteric bleeding resulting in amenorrhea. The same was true for 85 per cent of the metropathies.

RALPH A. REIS.

**Bowing, H., and Fricke, E.: Results Obtained by Irradiation of Carcinoma of the Cervix Uteri.** Journal-Lancet 51: 195, 1931.

The results obtained at the Mayo clinic by the irradiation treatment of cervical cancer are presented. The cases are grouped as follow: (1) early or operable, growth limited to cervical canal or part of the portio; (2) borderline, lesion involving the entire face of the cervix frequently with extension to the vaginal walls; (3) inoperable, infiltration of one or both parametria, frequently with fixation and "frozen pelvis"; (4) modified, the lesion modified by previous treatment elsewhere before the patient registered at the clinic; (5) recurring, recurrence following operation or irradiation at the clinic. Of the cases treated from 1915 to 1924 in-

clusive, 1001, or 91.5 per cent, of the total number studied were traced. Those living after five years constituted 75 per cent of the early group, 61.53 per cent of the borderline, 21.49 per cent of the inoperable and 24.82 per cent of the modified. Lesions were also graded according to Broder's classification. Those graded three and four showed a slightly better survival rate than those graded one and two.

FRANK SPIELMAN.

**deBuben, Ivan: Radium in the Treatment of Cancer of the Vagina.** Surg. Gynec. Obst. 52: 884, 1931.

As cancer of the vagina is a rare disease, there is not sufficient data on which to base a final opinion as to the value of radiotherapy.

Cancers of the vagina are exposed to a single dose of radium of 1,200 to 2,400 mg. hr. If examination shows an unsatisfactory result after six to eight weeks, the treatment is repeated. The lymphatic glands are treated with x-rays. Patients are examined once every six weeks for a while, then once every three months and later every six months.

The results obtained in the treatment of cancer of the vagina, whether by operation or by radiotherapy, are still far from satisfactory. The advantage of radiotherapy over surgery is that the latter has a wider range of applicability, also that at least temporarily its effect is palliative in most of the cases. The Wertheim method in patients who can be operated upon or total extirpation combined with the resection of rectum in cases with the growth in the posterior vaginal wall are considered to result in recovery most often. It is reasonable to hope, that by perfecting the methods of treatment and of the application of radium the results will not only be improved but the risk of recurrence will decrease.

WM. C. HENSKE.

**Petit-Dutaillis, P: Considerations of the Beginning, Evolution and Treatment of Vulvar Epitheliomas.** Based Upon Sixteen Observed and Treated Cases. Bull. de la Soc. d'obst. et de gynec. 10: 768, 1931.

Petit-Dutaillis reports 16 cases of vulvar carcinoma treated without any maternal mortality. In eight cases the epithelioma was limited to the vulva and there were no clinical manifestations of glandular involvement. Five of these cases were treated by total vulvectomy, two by total vulvectomy with subsequent radiation and one case was treated solely by means of radium. In eight cases the epithelioma had passed beyond the limits of the vulva. Two of these were treated by radium combined with surgery, whereas in the others only palliative treatment was given.

Vulvar carcinoma is one of the most serious forms of cancer and the incidence of cure is very small. Since in the author's series, half of the patients did not have any adenopathy it seems that vulvar cancer does not have any great tendency to extend to the lymph glands.

The author believes the best treatment for vulvar carcinoma is extensive removal of the vulva in a systematic way. Some individuals recommend a preliminary application of radium before operation. However, the author emphasizes that if radium is used, at least five or six weeks should elapse before the operation is performed. This is to prevent any unusual reaction in the cellular tissue and to avoid undue hemorrhage and lack of union of the sutures. However, the author does not believe the results obtained with preliminary radiotherapy justify its use. Certainly the loss of time involved should speak against it. Radiotherapy after operation however, is to be recommended.

J. P. GREENHILL.



Scott, E., and Oliver, M.: Primary Carcinoma of the Fallopian Tubes. *J. Lab. & Clin. Med.* 14: 429, 1929.

Since Webster's exhaustive article on primary carcinoma of the fallopian tubes in 1926, the authors have collected seven additional cases from the literature, and add two of their own. It is evident that primary carcinoma of the fallopian tubes is rare, and in comparison with the total pathologic lesions in this organ the percentage of malignancies is small. However, inasmuch as the condition is often recognized only histologically, cases certainly have been overlooked without microscopic examinations. Of the two cases reported, the first was a papillary alveolar carcinoma of the left tube and the second a similar carcinoma but not of the alveolar variety.

Both of these cases occurred in the postclimacteric period. The most common clinical symptoms of the disease are vaginal discharge, often bloody, pelvic pain, tumor mass and late in the disease, constipation and nocturia. The gross appearance of tubal carcinoma is often deceiving and its presence may be overlooked unless careful routine microscopic examinations are made. The microscopic picture is usually that of papillary alveolar carcinoma.

W. B. SERBIN.

# Item

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## AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY

The written examination of this Board held in various cities throughout the United States and Canada on October twenty-second consisted of the following questions.

1. Describe the circulation of the female pelvic organs.
2. What physiologic factors are responsible for the amenorrhea of pregnancy?
3. Describe the pathology of syphilis of the placenta.
4. Discuss the differential diagnosis of marginal and central placenta previa, and the treatment of the latter variety.
5. Describe the technic of internal podalic version and extraction.
6. What are the indications for cesarean section?
7. Discuss the use of pessaries in the treatment of retroversion of the uterus.
8. What are the contraindications for irradiation of fibromyomata of the uterus?
9. How do you treat carcinoma of the corpus uteri? Why?
10. Describe your operative technic in the removal of an intraligamentary cyst, 10 cm. in diameter, from the left broad ligament.

The general oral and clinical examination will be held in Los Angeles, December 7, 1932, immediately preceding the meeting of the Pacific Coast Society of Obstetrics and Gynecology. The names and address of successful candidates will be published in an early issue of the *AMERICAN JOURNAL OF OBSTETRICS AND GYNECOLOGY*.

The next written examination and review of case histories will be held in cities throughout this country and Canada, where there are Diplomates who may be empowered to conduct the examination, on April 1, 1933.

The next general, clinical examination is to be held in Milwaukee on Tuesday, June 13, 1933, immediately preceding the annual session of the American Medical Association. Reduced railroad rates will apply.

Early application is requested from those desiring to qualify for these examinations. For further information and application blanks address Dr. Paul Titus, 1015 Highland Building, Pittsburgh, Pennsylvania.

## Books Received

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CLINICAL ENDOCRINOLOGY OF THE FEMALE. By Charles Mazer and Leopold Goldstein. Illustrated. W. B. Saunders Company, 1932.

THE WISDOM OF THE BODY. By Walter B. Cannon, professor of physiology, Harvard Medical School. W. W. Norton & Company, New York, 1932.

THE HYGIENE OF MARRIAGE. By Millard S. Everett, Ph.D. Vanguard Press, New York, 1932.

PHYSIKALISCHE THERAPIE DER FRAUENKRANKHEITEN. Von Privatdozent Dr. Felix Gal, Zweite Universitäts-Frauenklinik in Budapest. Urban & Schwarzenberg, Berlin, 1932.

RECENT ADVANCES IN OBSTETRICS AND GYNECOLOGY. By Aleck W. Bourne and Leslie H. Williams. Third edition with 87 illustrations. P. Blakiston & Sons, Philadelphia, 1932.

SYNOPSIS OF GYNECOLOGY. By Harry Sturgeon Crossen, professor of clinical gynecology, Washington University Medical School, and Robert James Crossen, instructor in clinical gynecology and obstetrics. C. V. Mosby Company, St. Louis, 1932.

HANDBUCH DER INNEREN SEKRETION. Herausgegeben von Dr. Max Hirsch. I. Band, Lieferung 6. Curt Kabitzsch, Leipzig, 1932.

DER GEBURTSHILFICH-GYNAEKOLOGISCHE SACHVERSTAENDIGE. Von Privatdozent Dr. Paul Huessy. Hans Huber, Bern-Berlin, 1932.

RECENT WORK ON PTOSIS OF THE FEMALE PELVIC VISCERA. By E. Hesketh Roberts, gynecologic surgeon, St. Johns Hospital, London. With 30 roentgenographs in plates, two illustrations in text and two tables. Dickson & Scudamore, London, 1931.

STUDIEN UEBER DIE VERAENDERUNGEN DER NACHGEBURT BEI LUES. Von T. E. Olin, assistant der dermatologischen Klinik in Helsingfors. Gustav Fischer, Jena, 1931.

THE EXPECTANT MOTHER. By Frederick C. Irving, professor of obstetrics, Harvard Medical School. Houghton Mifflin Company, Boston and New York, 1932.

LES DIAGNOSTICS ANATOMO-CLINIQUES de P. Lecène. Appareil Génital de la Femme. Seconde Partie. Par P. Moulonguet. Masson et Cie, Paris, 1932.

FORMFEHLER UND PLASTISCHE OPERATIONEN DER WEIBLICHEN BRUST. Von Dr. Erna Glaesmer in Heidelberg. Mit 48 Abbildungen. Ferdinand Enke, Stuttgart.

DER KUENSTLICHE ABORT. Indikationen und Methoden. Von Professor Dr. Georg Winter, Königsberg, und Professor Dr. Hans Naujoks, Marburg. Ferdinand Enke, Stuttgart, 1932.

# American Journal of Obstetrics and Gynecology

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No. 6

## Original Communications

### THE RELATION OF PLACENTAL INFARCTS TO ECLAMPTIC TOXEMIA\*

A CLINICAL, PATHOLOGIC, AND EXPERIMENTAL STUDY

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*(From the Departments of Obstetrics and Pathology, respectively,  
Emory University School of Medicine)*

**R**OUTINE inspection of the placenta, on surface and on section, has impressed us with the fact that there is a close relation between the occurrence of placental infarcts and eclamptic toxemia.

The fact that infarcts occur more frequently in the placentas of toxemic patients has been recognized for some time. According to Williams, Fehling, in 1886, was apparently the first to call attention to the connection between albuminuria of pregnancy and placental infarction. Following this, and up to the time of Williams' article in 1900, there appeared reports of similar series of cases by Rouhaud, Cohn, Rossier, Cagny and Martin, in which the frequency of placental infarcts in cases of albuminuria varied from 33 to 85 per cent. Williams, in an examination of 500 placentas, found infarcts of all types present in 63 per cent, but analyzed the lesions from the standpoint of the etiology and the types and not according to their relation to toxemia.

Young, in 1914, stimulated a renewed interest in the relation of placental infarcts to toxemia, by his description of the earliest stages of infarct formation. He traced the changes in the lesion from the dark, congested, purple or almost black appearance in the early stage, to a lighter brick-red or brown color as the lesion became older, and then to a yellow and gray-white color in the final stage. He emphasized that the placenta from a fulminating type of eclampsia may show no other lesions than one or more dark, congested or purple-black areas in the substance. He obtained experimental support to his theory by injecting extract from artificially autolyzed placenta, subcutaneously, into guinea pigs and produced

\*Read, by invitation, at the meeting of the American Gynecological Society, May 31 to June 2, 1932, Quebec, Canada.

For lack of space it is not possible to print this paper in its entirety, but the complete paper may be had in the authors' reprints as well as in the current volume (1932) of the Society's Transactions.

NOTE: The Editor accepts no responsibility for the views and statements of authors as published in their "Original Communications."

muscular spasms, convulsions and death after several or more injections. Necropsy showed pathologic changes in the liver and kidneys very similar to those found in eclampsia.

\* \* \* \*

#### MATERIAL AND METHODS OF AUTHORS' INVESTIGATIONS

In order to follow up the suggestive clinical evidence of a relation between placental infarcts and eclamptic toxemia, the placentas from all deliveries from seven months on to full term were fixed from one to several weeks in 10 per cent formalin. Among these were occasional placentas from abortions of five or six months which were examined but not included in the series. The material was obtained from the obstetric services of Emory University Hospital (white) and Grady Hospital (colored). In each case the clinical record was obtained and notation made as to hemorrhage and particularly as to evidence of toxemia during pregnancy. The diagnosis of toxemia during pregnancy was based principally on albuminuria and a blood pressure in excess of 135 systolic and 85 diastolic, taken in conjunction with the usual symptoms of toxemia. The incidence of such cases was relatively much higher on the colored service, probably due to inaccuracies in the histories given by the patients and the greater prevalence of hypertension and albuminuria among colored patients, due to infected teeth and tonsils.

The placentas were cut in strips about 1 cm. in width and all lesions 5 mm. or more in diameter, were described as to location, size, color, consistency and composition insofar as could be judged from the gross appearance. Specimens typical of the various types of lesions were saved in formalin for microscopic examination. The microscopic appearance of each type of lesion was correlated with the gross appearance and with the clinical record.

Experimental support of the theory that the autolysis of placental infarcts is responsible for eclamptic toxemia, was sought through injections of Berkefeld filtrate of artificially autolyzed normal placenta into rabbits and guinea pigs. To determine whether autolysis of other human tissues would produce similar effect, the autolysates of liver and kidney were used.

A total of 1000 placentas was examined, the specimens being saved in consecutive order, 327 being obtained from the white service (private) and 673 from the colored service (charity). It was necessary, first to classify the various lesions, and inasmuch as such a classification must be based on the etiologic factors concerned, it will, first of all, be necessary to state our own views as to the cause of the lesions commonly called placental infarcts.

#### AUTHORS' THEORY AS TO ETIOLOGY AND EFFECT OF PLACENTAL INFARCTION

It is unquestionably true that certain placental lesions result from a physiologic endarteritis which becomes more marked toward the end of

pregnancy, as emphasized by Ackermann, Eden, Williams and others. This is not only readily demonstrated microscopically but can be easily recognized on close examination of the fresh placenta. By stripping away the amnion on the fetal surface of the placenta, over the vessels



Fig. 1.—Complete occlusion of villous vessel from physiologic obliterative endarteritis.

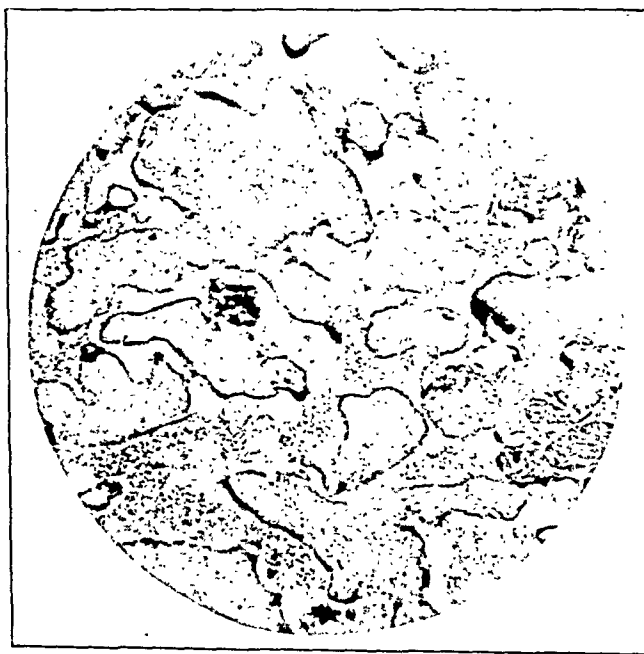


Fig. 2.—Hyalinization of villi resulting from very gradual obliterative endarteritis. Type 1 infarct, nontoxic.

leading to the infarcted area, one can usually demonstrate vessels which are entirely obliterated and appear as mere fibrous strands. Fig. 1 shows complete obliteration of a villous vessel. It is not at all difficult to find various degrees of partial obliteration of fetal vessels in sections from mature placentas.

The effect of this gradual shutting off of the circulation to the affected area is well described by Williams. There is a slow coagulation necrosis affecting the stroma and Langhans' layer, and later, the syncytium, which sets free products of necrosis, causing coagulation of maternal blood on the surface of the villi. In the early stages the nuclei are pyknotic but later on show karyorrhexis and karyolysis as a breaking up and finally a solution of the nuclear material takes place. If the circulation is diminished by very gradual stages, the entire villus and its branches, dependent on the affected vessel, apparently undergo hyaline change with formation of very little, if any, intervillous hyaline substance (Fig. 2). The absence of intervillous hyaline substance is probably accounted for by the extremely slight diffusion of products of

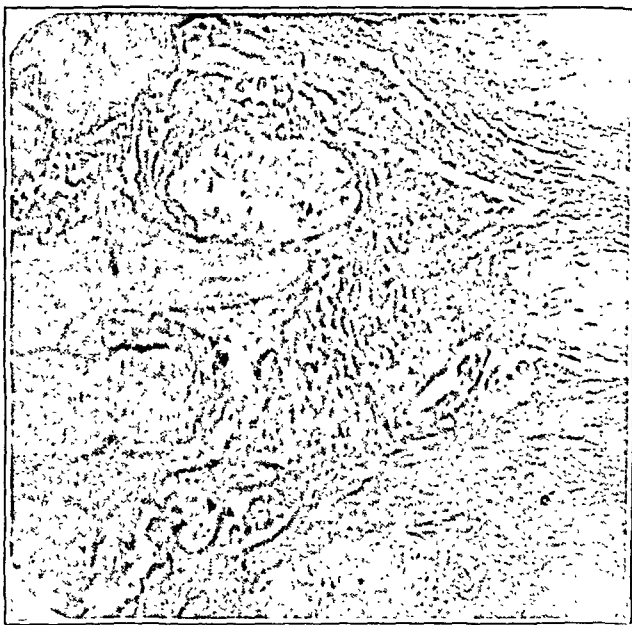


Fig. 3.—Pale "ghost villi" surrounded by dense hyaline intervillous substance resulting from obliterative endarteritis. Type 1 infarct, nontoxic.

necrosis, which do not reach sufficient concentration to cause coagulation of intervillous maternal blood. That hyalinization of the villi may progress without intervillous thrombosis is further favored by the fact that the syncytial layer which acts as an endothelium, is apparently more resistant to necrosis than the stroma or Langhans' layer.

If endarteritis proceeds somewhat more rapidly, the necrosis in the dependent villi is probably accelerated sufficiently to permit a more rapid diffusion of poisonous products and cause thrombosis in the intervillous spaces.

In this case, the coagulated maternal blood in the intervillous spaces takes on a hyaline appearance, the pale necrosed "ghost villi" becoming encased with deep staining homogeneous hyaline material in the early stages of necrosis of the villous stems, as shown in Fig. 3. Large masses

of villi are thus fused to form an infarct which derives its firm consistency and white appearance from the hyalinization and absence of circulation in the villi and intervillous spaces.

In this type of slowly developing infarct, we believe that the patient is protected against the poisonous products of autolysis of the placental protein by the fact that the gradual necrosis causes hyalinization of the villi or permits coagulation of maternal blood and formation of a protective zone of hyaline-like material around the villi, thus preventing the passage of poisonous products of villous disintegration into the maternal circulation. This accounts for the fact that firm, white infarcts may frequently be found in the placenta without any toxic manifestations.

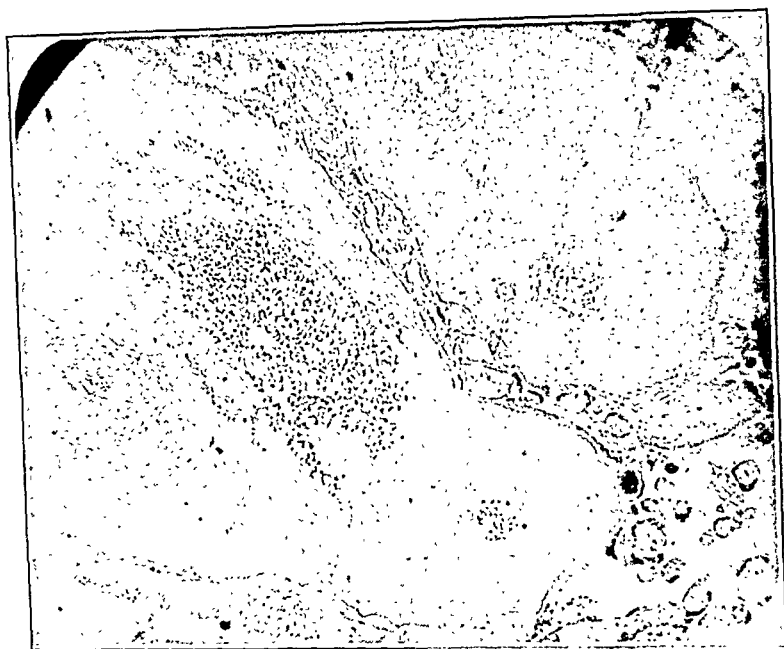


Fig. 4.—Extravasation of blood into stroma of villous stem, surrounding fetal vessel, probably due to trauma of fetal movements.

We believe there is another possible etiologic factor which may account for practically all other types of lesions. The trauma to which the fetal side of the placenta is subjected from the increasingly vigorous movements of the fetal extremities in the last two months of pregnancy must be taken into consideration. The force of these movements is considerable at times, as may be readily appreciated from palpation of the abdomen and from the evidence of pain shown by the patient. The placenta would probably receive more injury, were it not for the fact that it is usually situated on the anterior or posterior wall of the uterus, whereas, the natural position of the fetus is such that the fetal movements are usually directed to the right or left. If it is possible for a small superficial vein under the skin to be broken by a relatively slight trauma and result in an extravasation of blood in the tissues, it would



seem even more likely to occur on the fetal surface of the placenta, on account of the exposed and unprotected position of the fetal vessels. Furthermore, vessels which are undergoing endarteritic change would probably be more susceptible to injury.

At the site of the injury, thrombosis may occur with more or less rapid occlusion of the lumen, or a portion of such thrombus may easily become detached and occlude the main vessel or some of its branches. It is often possible to demonstrate a sudden diminution in the lumen of



Fig. 5.—Thick fibrin deposit beneath chorion on fetal surface of placenta, probably due to sudden rupture of fetal vessel from trauma of fetal movements.



Fig. 6.—Cut strips of placenta from fulminating eclampsia, showing dark areas of early infarction and area of hemorrhage in substance of placenta.

a vessel by stripping the blood back toward the center of the placenta. On releasing the pressure, the width of the returning blood stream may be seen to diminish suddenly to a fraction of its former bed without any apparent cause, such as an anastomosis or division of the vessel.

Further evidence is offered by the appearance of the vessels shown in Fig. 4. Extravasation of blood into the walls of the vessels is distinctly shown, an appearance which could hardly be produced by any other cause than trauma. Actual rupture of a vessel on the fetal surface of the placenta from the trauma of fetal movements would produce a considerable extravasation of blood under the amnion or chorion and might well explain the appearance shown in Fig. 5. The thick layer of fibrin

represents a former collection of blood from which the hemoglobin has been absorbed. Such an appearance has usually been attributed to the very slow circulation of the maternal blood beneath the fetal surface which predisposes to coagulation and the deposition of fibrin. Since a sluggish maternal circulation in this location is common, to all placentas, it would seem reasonable to expect to find deposition of fibrin in practically all specimens, but such is not the case. Large deposits, as seen in Fig. 5, are comparatively rare. Small, localized deposits are occasionally seen. Furthermore, the same supposed factor must be present in placentas of four or five months but we know that such collections of fibrin are seldom, if ever, found at this stage, when the fetal movements and endarteritis are considerably less marked.

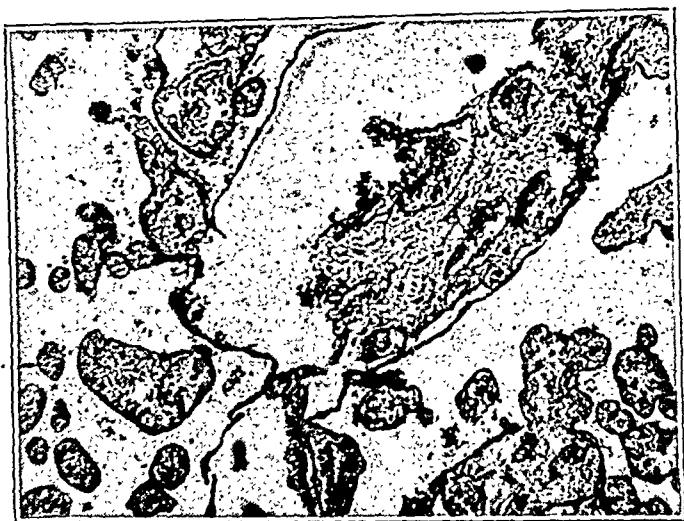


Fig. 7.—Photomicrograph from infarcts of placenta (Fig. 6), showing marked dilatation and rupture of villous capillaries and smaller vessels with acute necrosis of stroma, Langhans' layer and syncytium. Note absence of intervillous substance. Characteristic picture of preeclampsia and eclampsia.

If there is a sudden interruption in the circulation of a fetal vessel from rupture, thrombosis, or embolism, the area affected undergoes rapid degenerative changes. The gross appearance of acute lesions is shown in Fig. 6. The following is a brief history of the case:

S. R., colored, aged sixteen, primigravida; first prenatal visit seven months, November 18, 1931; blood pressure 104-68; no albumin; return visits November 25 and December 2; blood pressure not above 122-70; no albumin. Admitted to Grady Hospital January 22, 1932, false labor, blood pressure 120-86, apparently normal. Discharged January 23. Readmitted in coma, January 31, blood pressure 150-110, albumin 4-plus, many casts; severe headache preceding day; stupor and two convulsions just before admission. Treatment with glucose and magnesium sulphate intravenously. Labor induced by rupture of membranes. Normal delivery of living baby, weighing 2600 gm.; recovery.

The affected areas appear in the substance of the placenta as dark purple or almost black lesions in marked contrast to the surrounding normal red placental tissue. Coagulated or semifluid blood is seen in contact with some of these areas. The infarcted placental tissue still preserves its spongy, branching structure.

The microscopic appearance is shown in Fig. 7. A striking change is noticed in the appearance of the villous vessels and capillaries. They are markedly dilated and congested and some of the terminal capillaries are definitely ruptured, causing extravasation of fetal blood into the intervillous spaces. In some sections, both fetal

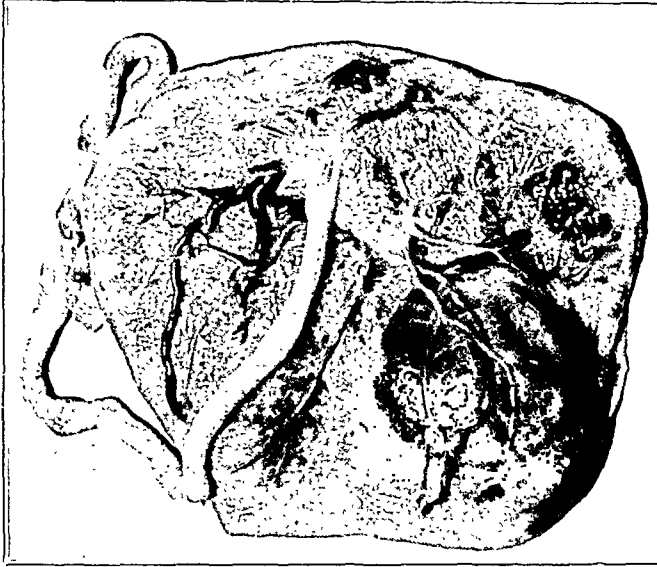


Fig. 8.—Placenta from fulminating eclampsia showing large subchorionic swelling due to hemorrhage under fetal surface of placenta, probably from trauma of fetal movements.

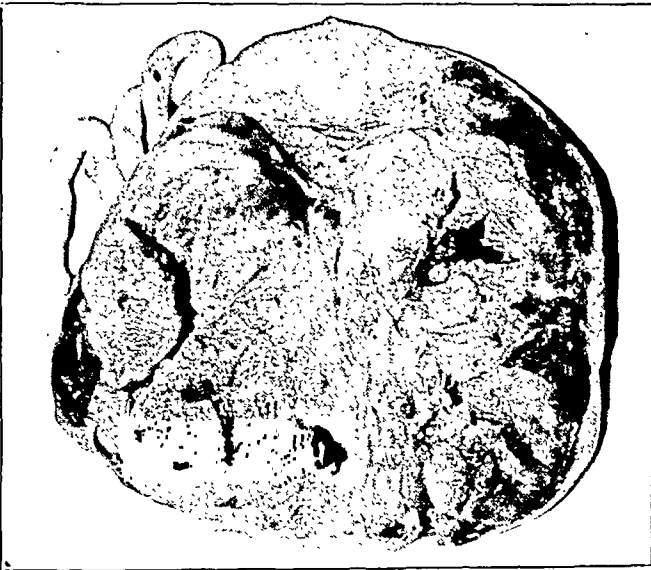


Fig. 9.—Rupture near center of maternal surface of placenta (Fig. 8) due to pressure of hemorrhage in substance of placenta.

and maternal blood cells can be seen in the intervillous spaces, due to a difference in the staining reaction. Thrombosis of some of the larger vessels may be seen. The stroma and Langhans' cells show early degenerative changes as evidenced by cloudy swelling, pyknosis and sometimes beginning disintegration. The syncytium appears to be more resistant, but pyknosis is usually evident in this layer also.

There is a striking absence of intervillous substance, and the maternal circulation between the villi is unobstructed. Consequently, the products of early autolysis, which are known to be exceedingly toxic, have free access to the maternal circulation.

The placenta from another case of fulminant eclampsia is shown in Figs. 8 and 9. The following is a brief history of the case:

Mrs. B., white, aged twenty-eight, primigravida, patient of Dr. A. S. Sanders; seen at office March 9, 1932, near end of seventh month, on account of headache.



Fig. 10.—Cut strips of placenta (Figs. 8 and 9) showing large brown infarcts in contact with main hemorrhage in substance of placenta. Lesion slightly older than those seen in Fig. 6.

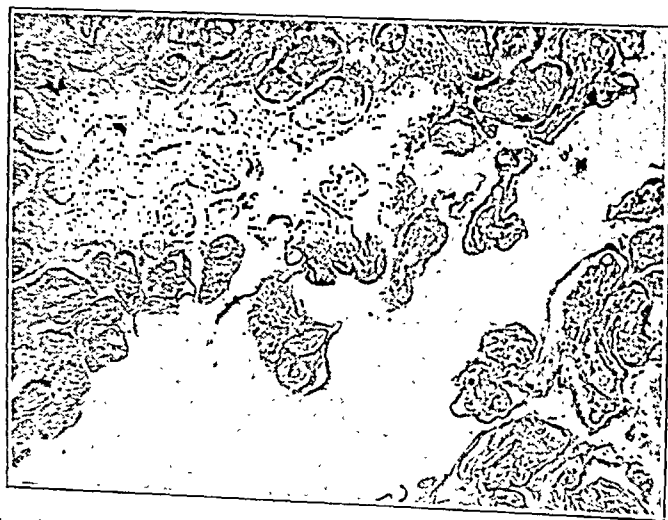


Fig. 11.—Photomicrograph from infarct shown in Fig. 10. Pathology same as shown in Fig. 7, except more advanced necrosis.

Blood pressure 125-80, slight trace of albumin. Restrictions of diet and exercise and increased catharsis advised. To return, March 14. Husband found patient unconscious on bathroom floor, 3 A.M. March 14. Three convulsions before admission to hospital. Blood pressure 140-90, albumin 4-plus, many casts. Labor induced by Voorhees bag. Normal delivery of living baby, weighing three pounds. Recovery.

There is a marked localized swelling about 8 cm. in diameter on the fetal side of the placenta. This is evidently due to sudden extravasation of blood from rup-

ture of a fairly large fetal vessel. The distention was sufficiently great to produce a star-shaped rupture of the placental tissue on the maternal surface. From the location and appearance of this hemorrhage, there is nothing to suggest its origin from rupture of a maternal vessel in the basal decidua or in a decidual septum between the cotyledons.

On section of the placenta, as shown in Fig. 10, several small, dark, spongy lesions are seen in the substance of the placenta, similar in appearance to those seen in Fig. 6, but the principal lesion is seen to be in contact with the area of hemorrhage, is more sharply defined and is of a dull chocolate brown color. The consistency is not spongy, but is more homogeneous and slightly firmer.

Microscopically, as shown in Fig. 11, different degrees of necrosis are seen, varying from pyknosis and cloudy swelling in the more recent spongy lesions, to extreme necrosis and disintegration with complete loss of staining power in the slightly older,



Fig. 12.—Cut strips of placenta from case of abruptio placentae showing infarcts exposed on maternal surface.

brown lesion. The villous capillaries are greatly dilated and congested. Many have ruptured. Thrombosis is seen in many of the larger vessels. There is practically no formation of intervillous hyaline substance. The color, demarcation, consistency and microscopic appearance mark the brown portion of the infarct as a slightly older lesion than in Fig. 6, and slightly more advanced in the process of disintegration and autolysis.

It is a well-known fact that abruptio placentae may occur, unexpectedly, in the course of preeclampsia and, conversely, that cases of abruptio placentae may unexpectedly develop eclampsia. Cases of abruptio placentae have been considered to be due to a toxin of a somewhat different nature than that causing eclampsia.

It has seemed to us that the process is essentially the same in both eclampsia and abruptio placentae and differs only in regard to the location of the infarct. If the lesion is in the substance of the placenta with intervening healthy placental tissue, separating it from the basal

decidua, the poisonous split-products of placental autolysis, of which histamine is probably one of the most active, are diffused through a wider intervillous circulation and are taken up by the decidual vessels of the entire placental site. In this case, the concentration of the poison is probably not sufficient to break down decidual sinuses and cause extravasation of blood with separation of the placenta. The pregnancy is therefore not interrupted at once and the general toxemia may reach such a degree that eclampsia occurs.

However, if the lesion is on the maternal surface, the concentration of the poisonous split-products of placental autolysis is brought to bear on the decidual sinuses in direct contact with the infarct and the effect, particularly of histamine, is probably sufficient to cause dilatation and



Fig. 13.—Photomicrograph from infarcts shown in Fig. 12. Pathology same as shown in eclamptic placentae.

rupture of the sinuses, extravasation of blood and separation of the placenta. In this case the pregnancy is usually interrupted before the general toxemia becomes marked enough to cause eclampsia. Since the infarction and the blood are of recent origin, the so-called "red infarct" has come to be recognized as a frequent accompaniment to abruptio placentae.

The appearance of such an infarct on the maternal surface of the placenta is shown in Fig. 12. The following is a brief history of the case:

Mrs. B., white, aged thirty-six, primigravida, patient of Dr. O. T. Malone, had an uneventful normal pregnancy until the sixth month. The blood pressure had not exceeded 115-70. Swelling of the feet began April 1, 1933, becoming generalized several days later. Severe headache and general malaise began April 8. Very little improvement from rest and other treatment. Marked increase in headache April 15. Severe cramp-like pains over lower abdomen, bleeding, nausea and vomiting, and marked dimness of vision April 16. Blood pressure 180-120. No convulsions. Spontaneous labor and delivery of stillborn, six months fetus. Large, firm clots ex-

pelled and placenta showed evidence of premature separation. Aching pain in region of liver April 19; numbness and weakness of left side. Blood pressure 150-100. Red blood cells in urine. Comatose condition April 20. Nonprotein nitrogen 173 mg. Urea 86 mg. Increased edema. Had five or six convulsions (uremic?). Died April 21. Necropsy. Brain convolutions flattened, suggesting increased pressure. No hemorrhage on surface. Liver showed numerous yellow areas on surface and section from few millimeters to several centimeters in diameter. Kidneys showed numerous hemorrhagic spots on stripping capsule. Marked engorgement. Microscopic examination: marked cloudy swelling, fatty degeneration, necrosis and scattered hemorrhages throughout liver lobules. Focal necroses with small round cell infiltration. Marked necrosis of renal epithelium, scattered hemorrhages, marked engorgement with free blood and numerous blood and hyaline casts. Glomeruli show marked engorgement and necrosis, acute hemorrhagic nephritis, and focal necrosis of liver.

The placental lesion is seen to be on the maternal surface. There has been some depression of the placenta in this region by the pressure of the clots which separated the placenta. The appearance of the lesion corresponds approximately to the dura-

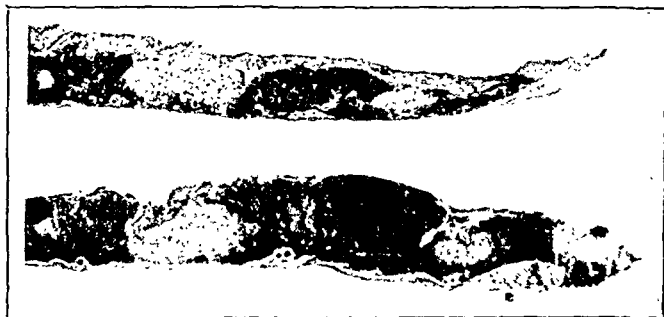


Fig. 14.—Strip of placenta from toxemia of three weeks' duration, terminating in eclampsia. Yellow, slightly softened infarct of subacute type near center and firm, white infarct from obliterative endarteritis on margin.

tion of the clinical symptoms, the affected tissue having a moderately firm consistency and light brown color.

Microscopically, as shown in Fig. 13, the villi show pyknosis, cloudy swelling and marked engorgement and dilatation of the capillaries in some areas; other villi show more advanced necrosis, disintegration and total loss of staining power, in the area bordering on the hemorrhage. The pathologic picture is the same as shown in Figs. 7 and 11, taken from the placental infarcts of the eclamptic cases.

Fulminating eclampsia and abruptio placentae do not occur as frequently as the gradually progressing type of toxemia of several weeks' duration, which eventually terminates in eclampsia, provided labor does not come on spontaneously or by artificial means. This type of toxemia is probably due to a more gradual or incomplete blockage of the circulation of a fetal vessel from thrombosis, possible rupture, embolism or even rapidly progressive endarteritis. By the time labor supervenes or is induced, the lesions have become yellow or dull gray and are well demarcated from the surrounding normal placenta. They lie mainly in the substance of the placenta but usually encroach to some extent on the maternal surface. Occasionally they may be situated on the edge

of the placenta, although in this location the lesion is usually of the non-toxic type and slow in development. Small succenturiate lobes are frequently the site of this type of infarct. There may be coagulated or semifluid blood, of a dull brick-red or brown color, in contact with the lesion. The consistency is homogeneous but only moderately firm and may yield scrapings to the knife.

The gross appearance of such a lesion is shown in Fig. 14. The following is a brief history of the case:

Mrs. B., white, aged twenty-four, primigravida, developed evidences of toxemia at the eighth month of pregnancy, with increasing edema, albuminuria, hypertension, and headaches. Within three to four weeks, blood pressure had increased to 170-110



Fig. 15.—Photomicrograph of subacute infarct shown in Fig. 14. Marked necrosis of villi and absence of intervillous substance.

and albumin 3-plus. Labor induced on account of preeclampsia. One convulsion during labor. Normal delivery, living baby. Recovery.

Microscopically, the appearance is shown in Fig. 15. The nuclei have lost their staining power. There is marked disintegration of the stroma, Langhans' layer and even the syncytium. In this area of the infarct the necrosis has been more rapid, coagulation of the blood in the intervillous spaces has probably been inhibited by anticoagulant toxic products, and the diffusion of the products of autolysis into the general circulation eventually reached such a concentration that eclampsia finally occurred. It is not uncommon in the subacute or slightly older lesions to find some variation in the extent of formation of intervillous hyaline substance, intervillous maternal circulation and degree of degenerative change in different parts of the same lesion (Fig. 16). Such variations in the pathologic process may account for the variations sometimes shown in the clinical features during the course of preeclampsia, as, for example, unexplained variations in blood pressure and albuminuria; unexpected improvement or rapid change for the worse.



Due to the fact that the subacute type of infarct is apparently associated with a progressive toxemia which ultimately results in eclampsia after several weeks or necessitates induction of labor, the lesion may not reach a healed quiescent stage, such as is seen in the firm, white lesions on the edge of the placenta resulting from slow physiologic endarteritis.

In addition to the infarcts heretofore discussed, which are made up chiefly of villi and intervillous blood or hyaline substance, certain other lesions are found which merely represent localized hemorrhages. In those of recent origin, the blood may be semifluid or appear as a soft, black clot. The villi are forcibly pushed aside as the blood clot forms. In hemorrhages of longer standing, striations of fibrin in fan-like arrangement may be seen, and the color gradually becomes a lighter red or brick color as the red cells break down and the hemoglobin disappears. Eventually the fibrin alone remains, giving the lesion a yellow

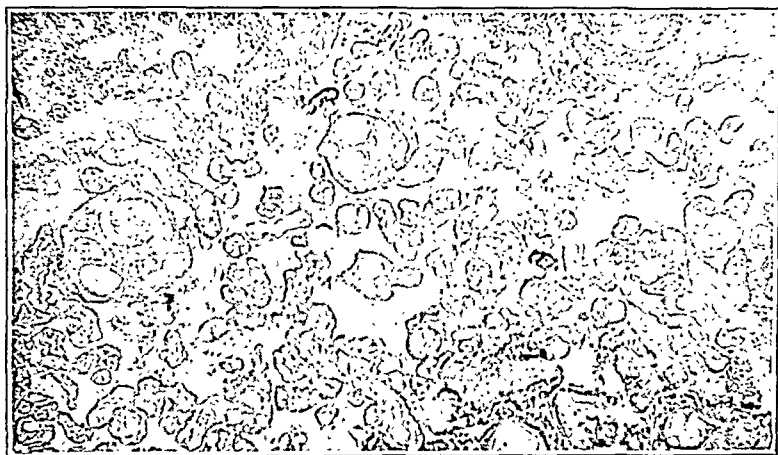


Fig. 16.—Photomicrograph from subacute placental infarct from case of moderately severe toxemia. Upper deep staining zone is oldest and shows partial formation of intervillous substance; light zone shows dilated, ruptured villous vessels, necrosis, thrombosis and open intervillous spaces; lower zone shows more recent involvement.

or gray white appearance. The consistency is rather soft and the fibrin can be broken away in flakes or layers.

Certain hemorrhagic areas seem to contain sufficient anticoagulant substance, such as peptone body, probably from some degree of necrosis of villi on the border of the area, to remain semifluid. Fibrin is absent or very limited, and through absorption of hemoglobin the contents become gelatinous or cystic. Complete absorption of the contents may possibly account for the open spaces occasionally seen in the placental substance, which Hartmann and Siddall have attributed to bacterial action after delivery.

A large proportion of the hemorrhagic and fibrinous areas is found under the fetal surface or in the placental substance. They are separated from the basal decidua by intervening healthy villi and normal intervillous maternal circulation. While it is difficult to prove the origin of these areas, we believe they arise either from traumatic

rupture of a main villous vessel or from the dilatation and rupture of the capillaries of the terminal villi, following traumatic thrombosis of this main vessel. It is difficult to explain their origin from rupture or obstruction of maternal vessels in the basal decidua or in the decidua septa. Our conception of the sinus-like circulation at the placental site and the unusually free communication between the villi, argues against the possibility of any portion of the placenta being entirely cut off from maternal blood.

\* \* \* \*

It is our belief, therefore, that all placental lesions, excepting some of the gelatinous areas, may be attributed to interference with the fetal circulation which may be brought about either in a gradual manner from physiologic endarteritis or in an abrupt manner from actual vascular rupture, thrombosis or embolism produced by the trauma of fetal movements.

The infarcts of acute or subacute development are probably responsible for eclampsia and abruptio placentae according to whether they are situated in the substance or on the maternal surface of the placenta. Infarcts of slow development are seldom if ever responsible for toxemia.

#### CLASSIFICATION AND FREQUENCY OF PLACENTAL LESIONS

The following description of the essential features of the lesions found in our own series corresponds closely to that given by Hartmann and Siddall in their own study:

*Type 1.*—Oval or round lesions, usually from one to several centimeters in diameter; white or pearly gray; of firm consistency; compact; nonstriated; usually situated near or on the border of the placenta and on the maternal surface; calcification may be present. Microscopically: pale necrosed villi fused by homogeneous deep staining hyaline intervillous substance. Villous vessels not dilated or ruptured.

This type of infarct is the result of physiologic endarteritis and is of no importance from the standpoint of eclampsia. It was found in 40 per cent of the white cases and 38 per cent of the colored.

*Type 2.*—Oval or round lesions, one to several centimeters in diameter; light pink, red, dark brown, or black; occasionally striated; usually situated in the placental substance. Microscopically: red blood cells and lamellae of fibrin; no villi.

This type of lesion is a true hemorrhage resulting from rupture of a fetal vessel or capillary, directly or indirectly from the trauma of fetal movements. It was found in 12.5 per cent of the white cases and 11.5 per cent of the colored. Toxemia will depend on the degree of secondary necrosis of villi dependent on the vessel or bordering on the hemorrhage.

*Type 3.*—Oval or round lesions, one to several centimeters in diameter, gray or white, occasionally slightly pink; striated or in lamellae, usually situated in the substance of the placenta but frequently under the fetal

surface. Microscopically: mainly fibrin layers; occasionally degenerated red cells; no villi.

This type is apparently a late or final stage of Type 2 lesion, in which the red cells have disintegrated and the hemoglobin has been absorbed. It was found in 5.5 per cent of the white cases and 6 per cent of the colored. Not primarily associated with toxemia.

*Type 4.*—Round or oval lesions, one to several centimeters in diameter, dark purple in the acute form, brown to yellow in the slightly older forms, soft and spongy in the acute stage but homogeneous and slightly firmer in the subacute stage; situated in the mid or outer zone of the placenta and usually in the substance or on the maternal surface of the placenta; lesion is often in contact with semifluid blood or clot. Microscopically: villi in various stages of necrosis, more advanced in brown or yellow lesions; villous capillaries and veins markedly dilated and distended in acute forms, less in subacute; occasionally ruptured; engorgement causes villi to appear more crowded; very little, if any, formation of hyaline intervillous substance. Thrombosis of villous vessels frequently seen.

This type is a true infarction resulting from rupture of a fetal vessel or occlusion from thrombosis or embolism, from the trauma of fetal movements and is probably the cause of abruptio placentae and eclamptic toxemia. It was found in 4.2 per cent of the white cases and 4.8 per cent of the colored.

*Type 5.*—Irregularly shaped, round or oval lesions somewhat smaller than the other lesions, transparent or slightly opalescent, occasionally slightly pink; some apparently encapsulated, others bordering directly on villi and always in placental substance. Microscopically: structureless, homogeneous material, occasionally surrounded by capsule of decidual cells; no villi. These lesions may represent degeneration of decidual septa; in other cases apparently the final stage of a hemorrhagic area in which fibrin formation was possibly inhibited by a peptone split-product. This type of lesion is of no clinical significance.

Although we agree with Hartmann and Siddall as to the essential features of the four types of lesions, there is a considerable difference of opinion as to the incidence of each type of lesion. In our own series we are certain we have overestimated Type 1 and underestimated Type 3 by relying too much on the appearance and too little on the consistency of the lesion. Greater familiarity with the types of lesions will eliminate differences in interpretation.

In our white series there were 34 cases of toxemia. In these cases, infarcts of Type 1 were twice as frequent and infarcts of Type 4 were almost eight times as frequent. Types 2 and 3 showed only a slight increase. This agrees with Hartmann and Siddall's findings in toxemic cases, and lends support to the theory that the more rapid necrosis and autolysis of placental infarcts are responsible for eclamptic toxemia.

In the early part of our study, we were not sufficiently familiar with the early stage of the Type 4 lesion, and consequently classified some eclamptic placentas as negative because of the absence of yellow or gray soft necrotic lesions which represent the later stages of the Type 4 lesion, and are more characteristic of a subacute toxemia. Since learning to recognize the dark purple, spongy, or brown, slightly firmer lesion of acute toxemia, a definite pathologic basis, both in gross and microscopic examination of the placenta, has been found in all cases of pre-eclampsia, eclampsia, and abruptio placentae.

#### EXPERIMENTAL BASIS FOR THEORY OF PLACENTAL AUTOLYSIS

If eclamptic toxemia is due to poisonous split-products of placental protein, it should be possible to produce the clinical and pathologic



Fig. 17.—Photomicrograph of liver of guinea pig, showing congestion, areas of hemorrhage in mid and outer zone of lobule, fatty degeneration, cloudy swelling and necrosis. Convulsions and death from injections of autolyzed placenta.

manifestations of the disease by the injections of artificially autolyzed placental tissue into susceptible animals.

\* \* \* \*

#### AUTHORS' EXPERIMENTS

In our first experiment, fresh normal placenta was washed free of blood, ground thoroughly, covered with toluene and allowed to autolyze in the incubator at 37° C., for four hours. The toluene was then removed and sterile physiologic-saline solution was added in the proportion of 1-5, and 0.5 per cent tricresol added as a preservative. The preparation was allowed to undergo extraction in the refrigerator for ninety-six hours. The solution was then passed through a Berkefeld filter to insure sterility and the removal of any solid particles before injection.

A rabbit was given intravenous injections of 1 c.c. daily until 10 c.c. had been given. The animal showed no unusual symptoms during the period of the injections or for a period of twenty days thereafter. At the end of this time necropsy was done. The epithelium of the tubules showed marked cloudy swelling, disinte-

gration and desquamation. Hemorrhage was present both between and into the tubules and the glomeruli showed marked congestion and slight hyalinization. The liver showed marked congestion of the bile capillaries and hemorrhages toward the center of the lobules as well as in the periphery. The liver cells showed marked cloudy swelling.

In a second experiment, guinea pigs were used and normal placenta was prepared in the same manner, except that one portion was allowed to autolyze under toluene in the incubator for four hours and another portion for ninety-six hours.

A guinea pig was given four intracardiac injections of 0.5 c.c. of the four-hour preparation, at daily intervals, followed by seven subcutaneous injections of 0.5 c.c. daily. Another guinea pig was injected in the same manner with the ninety-six-hour preparation. Three days after the last subcutaneous injection, both guinea pigs

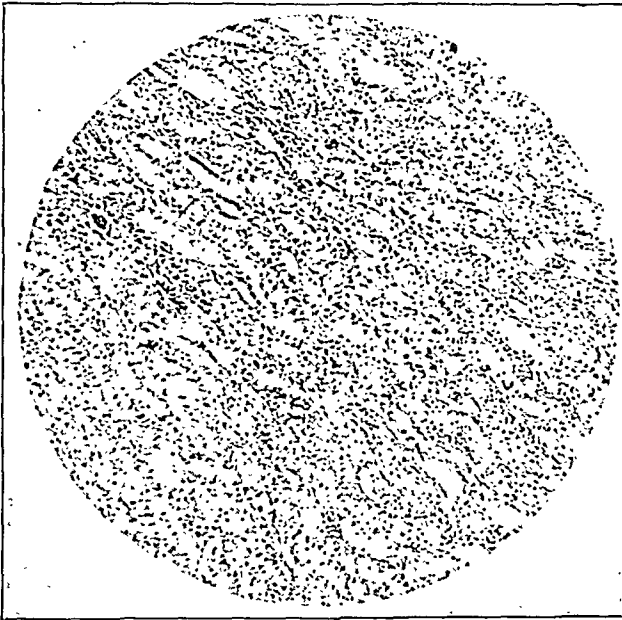


Fig. 18.—Photomicrograph of kidney (same guinea pig) showing cloudy swelling, necrosis, desquamation of epithelium of tubules, congestion and small hemorrhages between and into tubules.

developed intermittent convulsive seizures, continuing for two hours until death occurred.

The liver cells of the animal receiving the four-hour preparation showed cloudy swelling, marked fatty degeneration and necrosis throughout the entire lobule. Small hemorrhages were present between the liver cords, more marked near the central vein than in the periportal region (Fig. 17).

The tubular epithelium of the kidney showed marked cloudy swelling, disintegration and desquamation. Considerable hemorrhage was present between and into the tubules. The glomerular tufts were engorged with blood which showed early hyalinization and the glomerular epithelium showed pyknosis (Fig. 18).

The liver cells of the guinea pig receiving the ninety-six-hour preparation, showed cloudy swelling involving the entire lobule, distention of the bile capillaries and occasional extravasation of blood.

The tubular epithelium of the kidney showed pyknosis, cloudy swelling and complete destruction of some of the tubules. Hemorrhage into many of the tubules was seen. The glomeruli were apparently normal.

Apparently the products of the four-hour are much more toxic than those of the ninety-six-hour autolysis, which bears out Wells' statement that the products from the early stage of cell necrosis have the greatest toxicity. Chemical changes apparently occurred in the ninety-six-hour preparation, which rendered the products somewhat less toxic to the kidneys and liver, but sufficient to cause convulsive seizures. It is also interesting to note that convulsions did not occur until three days after the last injection.

In a third experiment, extracts were made from ground human liver. A guinea pig was given twelve injections of 5 c.c. each, of a twenty-four-hour autolysate, four of which were given intracardially and eight subcutaneously. Three days after the last injection, the guinea pig was found dead. The liver and kidneys showed essentially the same pathologic picture of marked cloudy swelling, necrosis and hemorrhages as seen in the guinea pigs receiving placental autolysate, except that fatty degeneration in the liver was somewhat less marked than that found resulting from the four-hour placental autolysate.

To determine whether a difference in the clinical and pathologic effects of normal areas and infarcted areas in a placenta from eclampsia could be demonstrated, equal quantities of the normal and the brown infarcted areas from the placenta shown in Fig. 10 were ground in sand and diluted with sterile, normal saline in the proportion of 1 to 5. Tricresol (0.5 per cent) was added as a preservative and the suspension allowed to extract in the refrigerator for forty-eight hours, and then passed through a Berkefeld filter to insure sterility. Guinea pigs were given a daily dose of 1 c.c. subcutaneously, until a total of 20 c.c. had been given. There was apparently no effect on the animals except for some loss of weight. Necropsy was done and the liver and kidneys examined. Pathologic changes were noted similar to those found in the guinea pigs having convulsions, although not so extensive. No marked difference was noted in the effects produced by the normal and the infarcted placental tissue. Inasmuch as the entire placenta was subject to autolysis at intervals during a period of eighteen hours when photographed and examined, the results cannot be taken as evidence against an increased toxicity of the infarcted areas. It is believed that the above experiment, if carried out at once after delivery of the placenta, would show a definite increase in toxicity of the acute infarcts.

It is evident, therefore, that the protein split-products of placental autolysis when injected intravenously or subcutaneously into guinea pigs or rabbits produce poisonous effects, which, both clinically and pathologically, are very similar to those of eclampsia. Objection has been raised by Seitz, Williams and others that similar effects can be obtained by the injection of extracts from autolysis of other organs as well as placenta and also that the injection of unautolyzed placental extract is without effect. In our opinion, this does not constitute any objection whatsoever to the theory of the origin of eclampsia from the products of placental autolysis, since we are probably dealing with protein split-products common to all tissues.

## BIOCHEMISTRY INVOLVED IN AUTOLYSIS OF PLACENTA

All tissues during the process of necrosis and autolysis, whether in vivo or in vitro, yield protein split-products which are common to all and are highly toxic. The very cellular tissues such as liver, kidney, spleen, pancreas, etc., autolyze more rapidly and completely and yield more poisonous products than muscle or fibrous tissues. The clinical conditions under which we may have extensive autolysis going on in the body at such a rate that the concentration of the poisonous products overtaxes the natural detoxifying mechanism are relatively few, but the clinical and pathologic effects of severe burns, severe crushing injuries, gangrenous intestine, pancreatic necrosis, acute yellow atrophy of the liver, etc., strongly suggest the overwhelming of the body defenses by highly poisonous protein split-products.

As to the nature of these poisonous split-products, we may gain some information from analyses of placental tissue which have been made by Koelker and Slemons and by Harding and Fort. The latter investigators found the nitrogen content 14.7 per cent, water 9.5 per cent, ash 5.07 per cent, and fat 1.15 per cent. The nitrogen distribution was as follows: amid 6.34 per cent, humin 3.20 per cent, arginine 24.08 per cent, histidine 2.32 per cent, lysine 7.34 per cent, and cystine 1.47 per cent. Total diamino 35.20 per cent, monamino 51.5 per cent, and nonamino 3.47 per cent. Total recovered 99.89 per cent.

They call attention to the strikingly high content of arginine in the placenta, which is about twice that of other organs, and consider that it may be related to the special function of the placenta as an organ of nutrition to the fetus.

According to Wells, all tissues possess the power of self-digestion or autolysis, by virtue of proteases present in every cell. There are two intracellular proteases—one resembling pepsin, which carries digestion to the peptone stage and requires an acid medium of optimum  $P_H$  4.5 to 3.5; the other resembling ereptase, splitting peptones and peptids into amino acids, with optimum  $P_H$  7.8 and not inhibited by acid reaction above  $P_H$  3.\*

\* \* \* \*

Histamine is produced by the decarboxylation of the amino acid histidine. It occurs in extracts of all tissues, occasionally free, but usually liberated by protein cleavage by acids, ferments or bacteria, particularly of the colon group. It may be extracted with water, saline or dilute alcohol and retains its potency for long periods at ice box temperatures.

\* \* \* \*

A striking similarity to many of the effects of histamine, is seen in the acute, severe cases of abruptio placentae complicated by toxemia. The circulatory manifestations are seen in the frequent occurrence of shock, low blood pressure, nausea, vomiting, occasionally of dark bloody vomitus, spasm of the uterus, edema, and hemorrhages on the surface and between the muscle fibers of the uterus and at the placental attach-

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\*The blood is  $P_H$  7.4 to 7.8.

ment. A moderate amount of blood tinged fluid is often found in the peritoneal cavity.

\* \* \* \*

Peptones render the blood noncoagulable when injected into the circulation. This is most significant inasmuch as certain cases of abruptio placentae may show a delayed coagulation time. Mrs. N. developed an acute toxemia during the eighth month of pregnancy. Abruptio placentae developed, and on admission to the hospital the blood pressure was 195-115. Death occurred from toxemia and persistent hemorrhage several hours after a spontaneous labor and delivery, transfusion and other treatment being of no avail. The coagulation time could not be obtained, a specimen of blood standing seventeen hours without showing any evidence of clotting. Needle punctures from hypodermics bled persistently and there was vomiting of dark bloody material during labor. The blood calcium was found to be 7 mg., considerably less than the normal value. There were no platelets. A soft, brown yellow infarct showed the characteristic picture of acute necrosis, disintegration and absence of intervillous substance.

\* \* \* \*

CORRELATION OF BIOCHEMICAL AND HISTOLOGIC CHANGES IN ACUTE AND  
SUBACUTE INFARCTS WITH THE CLINICAL FEATURES OF ECLAMPTIC  
TOXEMIA AND ABRUPTIO PLACENTAE

Wells studied the relation of autolysis to the histologic changes. There is first a decomposition of the nucleoproteins of the nuclei which is probably brought about by intracellular autolytic enzymes. This is evidently responsible for the deeper staining reaction of the nuclei, the liberated nucleic acid having a greater affinity for the basic stain, and giving the appearance termed pyknosis. Later, the nucleic acids are further decomposed through special enzymes, the nucleases, which probably accounts for the gradual loss in staining power.

\* \* \* \*

Considering the variety of protein cleavage products, with various effects such as inhibition of coagulation, vasodilation, vasoconstriction, agglutination of red cells, toxic effect on vessel walls permitting escape of corpuscles and plasma, spasm of the uterus, etc., it is more readily understood why we may have eclampsia without definite convulsions, eclampsia without much if any elevation of blood pressure, shock, variations in degree of albuminuria or edema, the unexpected occurrence of abruptio placentae in the course of what is considered preeclamptic toxemia or the occurrence of eclampsia in the course of what appears to be abruptio placentae, or even nephritic toxemia. It is also probable that histamine or products closely related to it not only account for abruptio placentae but also for the occasional development of edema of



the lungs and petechial hemorrhages in the brain of the eclamptic patient.

It is also clear why the main pathology of eclampsia is seen in the liver, the chief detoxifying organ of the body, and that the pathology in the kidneys supports the view, as stated by Bell, that 'a soluble toxic substance in the blood is responsible for eclampsia.

\* \* \* \*

If the above theory as to the cause and effect of placental infarction and autolysis is proven to be correct, through further clinical, pathologic, experimental and biochemical investigation, it holds out no hope for the control of infarct formation, but emphasizes the imperative need for close observation of patients who develop definite evidence of toxemia, and the necessity of prompt interruption of pregnancy if the toxemia increases. A more specific and effective treatment will be developed only through biochemical research in the recognition and neutralization of the poisonous products of placental autolysis.

#### CONCLUSIONS

1. Placental infarcts are probably due either to gradual interruption in the circulation of a fetal vessel from the physiologic endarteritis characteristic of the latter months of pregnancy, or to an abrupt interference as a result of rupture, thrombosis or embolism of a fetal vessel, brought about by the trauma of fetal movements on the unprotected fetal vessels on the surface or in the substance of the placenta. Disturbances in the maternal circulation are probably secondary and not primary.

2. Infarction is followed by necrosis and autolysis of the affected placental tissue, thereby liberating poisonous protein split-products such as peptone, histamine, tyramine, guanidine, etc., by virtue of the proteases present in all cells.

3. The physiologic and pathologic effects of these substances are strikingly similar to the clinical and pathologic findings in eclampsia.

4. Slow necrosis, due to physiologic endarteritis, permits thrombosis and the formation of a protective zone of hyaline intervillous substance about the affected villi, thus preventing the diffusion of poisonous protein split-products into the maternal circulation. The villous vessels show very little if any dilatation or engorgement. Such infarcts are firm and white and are not responsible for toxemia.

5. Acute necrosis is probably due to rupture, thrombosis or embolism in a fetal vessel, from trauma of fetal movements. The affected areas first appear dark and spongy, but soon become slightly firmer and of a brown color. Microscopically, the villi show necrosis with congested, dilated or ruptured capillaries and thrombosed vessels. The striking absence of intervillous hyaline substance is probably due to the liberation

of peptone, which has an anticoagulant effect and thereby permits the diffusion of poisonous protein split-products into the maternal circulation, resulting in eclampsia.

6. Toxemia of gradual development, over a period of several weeks, eventually resulting in eclampsia probably differs only in a more gradual necrosis with more evidence of hyaline intervillous substance, and less marked dilatation of villous capillaries and veins. The circulation is probably not completely obstructed. The infarcts in this type are yellow to gray, somewhat soft and are more definitely demarcated.

7. Eclampsia and abruptio placentae probably differ only in the location of the infarcts. In eclampsia, the infarcts are in the substance of the placenta. The intervening healthy placental tissue serves to diffuse the poisonous products, and prevents sufficient concentration of histamine to rupture the decidual sinuses and separate the placenta. Hence, pregnancy continues until eclampsia occurs. If the infarct is in contact with the decidual sinuses, histamine probably brings about abruptio placentae before eclampsia can occur.

8. Injections of Berkefeld filtrate of artificially autolyzed normal placenta into guinea pigs produces stupor, convulsions and death. The pathologic changes in the kidneys and liver are similar to those found in eclampsia. The fact that the injection of autolysates of other organs may produce similar effects in the liver and kidneys of an animal, does not disprove the placental theory of eclampsia, but indicates that the pathologic effects are due to protein split-products common to all tissues, varying somewhat according to the chemical composition of the tissue.

9. It is probable that with a better understanding and recognition of the acute and subacute types of placental infarcts, the association of the same, with preeclampsia, eclampsia and abruptio placentae will be found to be quite constant.

10. If autolysis of placental infarcts is the cause of eclamptic toxemia, it follows that until the specific protein split-products can be successfully recognized and neutralized, emphasis must continue to be placed on prompt interruption of pregnancy before convulsions are threatened.

*(For discussion, see page 937.)*

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# RESEARCHES ON THE TOXEMIAS OF LATER PREGNANCY\*

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## THE DIETETIC FACTOR

ECLAMPSIA is a controllable, or partially controllable disease. We are not referring to the decrease in eclampsia noted in prenatal clinics, where the expectant mother is watched monthly or even weekly for any signs of the onset, and where treatment is promptly instituted should any signs be forthcoming. We refer to that great scale experiment in the world war, where the incidence of eclampsia fell from 14 in 1000 to 9 in 1000, in all the big centers of the Central Empires. Even in the postwar period the incidence rose only to its prenatal level, when owing to the greater number of primiparous births it should have been higher. To what cause is this diminution due? The majority of the German and Austrian<sup>1</sup> observers attribute it to the lessened intake of protein and fat. Sweden<sup>2</sup> showed a similar decrease, though Russia,<sup>3</sup> where extreme famine conditions prevailed during the same years, showed an increase.

It has always been a moot question with us that either of these two dietary constituents plays a part in the production of a toxemia of pregnancy. We have not come across one single controlled observation showing that the inclusion of protein or fat in a diet in pregnancy brings on, either an eclamptic seizure, or preeclamptic signs. Those who state that the withdrawal of protein or fat has caused a diminution in preeclamptic symptoms must show strictly the absence of other changes, not only in the diet, but in environmental factors, likely to act favorably. It is not sufficient to conclude that because a carbohydrate diet or a milk diet, given in hospital or even in home treatment, produces good results, that those results are due to a withdrawal of protein or fat. Indeed in proportion to its calories milk contains a large amount of both. Probably the close associations of eclampsia with nephritis, and the older ideas that protein was harmful in the latter disease, resulted in the adoption of a similar view in the toxemias of pregnancy. One notes however, in many centers, that moderate amounts of protein are now allowed. In view of these doubts we proceeded to carry out a series of observations in pregnancy. We proceeded cautiously. We gave normal pregnant women diets high in protein, fat or carbohydrate, but salt-poor (See Tables I and II). The women were under daily supervision in the metabolism ward, and during the period of

\*Read, by invitation, at a meeting of the New York Obstetrical Society, February 9, 1932.

dieting were kept in bed. Our results were entirely negative. Neither protein, nor fat produced any symptom of any kind. Carbohydrate was not expected to cause disturbance. In this series of observations it acted merely as a control diet. Our observations and conclusions were not unexpected. Burger,<sup>4</sup> a little time previously, had fed normal pregnant women diets containing 200 gm. of protein without observing any ill-effects, and there must be many women who during gestation take protein in amounts similar to our diets, and remain entirely normal. Clinically it is also of interest to note that not one of our patients suffered from nausea or

TABLE I. DIETS USED IN NORMAL AND TOXEMIC PREGNANCIES

	HIGH PROTEIN	HIGH CARB.	HIGH FAT	
			1	2
Protein, gm.	118	30	46	42
Fat, gm.	38	34	138	104
Carbohydrate, gm.	185	304	57	38
Calory Value	1595	1687	1667	1235

TABLE II. DETAILS OF HIGH PROTEIN DIET

BREAKFAST		DINNER		SUPPER	
	gm.		gm.		gm.
Oatmeal Porridge	60	Scraped Beef	140	Scraped Beef	90
Sugar	10	Potato (boiled)	70	Baked Beans	110
Milk	50 c.c.	Bread	70	Bread	60
Boiled fresh cod	85	Butter	8	Butter	7
Toast	70	Gelatin (diabetic)	1 pkg.	Baked Apple	60
Butter	8	Milk	230 c.c.	Sugar	5
Milk	211 c.c.			Milk	230 c.c.

vomiting when on the high fat diets though some were showing a high degree of "acetone" production. Ketosis will not produce nausea and vomiting of pregnancy.

Our next step was to feed the same diets to patients with mild toxemia.<sup>5</sup> Clinically our patients might have been classified in many ways, hypertension, low kidney reserve, nephrosis, nephritic toxemia, pre-eclampsia, etc. They were cases however, which would have been subjected to purgation, then given water and afterwards a milk diet, under the ordinary routine of hospital treatment. No purgation was employed. The bowels were emptied daily by simple enemas, which was supplemented by a mild cathartic if necessary. At that time it was our opinion that the semistarvation of such a routine was injurious to the general well-being of the patient. Calories if not supplied in the food, inevitably come from the patient. At no time however did we overstep the patient's calory requirements. The diets contained the minimum amount of salt. Clinically the results were satisfactory. Edemas, hypertensions, albuminurias, all subsided. We should like to point out that at no time have we recommended these diets as specifically curative, or insisted on their

use. Our object was purely demonstrative. The choice of diet can be left to the obstetrician or internist in charge. We merely point out that the choice at his disposal is wide, and fail to see why the patient need live so extensively on her own tissues. Bland and Bernstein<sup>6</sup> also have advocated salt-free diets. They attempted to minimize the factor of hospitalization in their results by keeping the patients in bed on ordinary diet, and allowing them out of bed on the salt-free diet. It was in this latter period that improvement took place. Plass<sup>7</sup> recently has also convinced himself of the innocuousness of protein in the causation of the toxemias of later pregnancy.

What happens when a liberal amount of salt is included?

Everyone is aware of the connection between salt and edema. The work of Ambard, Weil, etc., is well known. All clinical workers know the value of salt-poor diets in the treatment of the edema of nephrosis and of cardiac decompensation. It is known too that the offending part of the salt is the sodium and not the chlorine ion. Other chlorides have no action in producing edema. Other sodium salts, such as bicarbonates and salicylates have this action. The French group of clinicians however had also claimed that a high salt diet was responsible in part for hypertension, and in this country Allen<sup>8</sup> vigorously championed the idea, though later he was compelled to acknowledge the ineffectiveness of salt-free diets in all types.

The normal pregnant woman behaves to a sudden intake of sodium chloride in a perfectly definite manner.<sup>9</sup>

In Table III is shown the approximate water and chloride balance during the seventh, eighth, and ninth day of one of our high protein and carbohydrate diets, on 2 normal pregnant women. It will be seen that the chloride output is approximately 3 gm., and there is an approximate water balance. On the tenth, eleventh, and twelfth day, without any other change in the diet 15 gm. of sodium chloride was added. At once there is a large positive water and salt balance. The body continues to gain water and salt on the next day, though not so greatly, and by the third day of the high salt intake, the equilibrium is nearly complete. What has happened to the water and salt retained by the patient? Blood analysis shows that the blood has become hydrated. The serum proteins have fallen, and the chlorides have risen. Some salt solution evidently has been retained, and the plasma has become diluted. Clinically the patient shows thirst on the first and second days of the high salt intake, but when equilibrium is established the thirst disappears. Occasionally we have caught a fleeting impression of edema in the legs on the first or second day of the high salt intake. Thus the normal pregnant woman adjusts herself to a high salt intake. The nonpregnant individual behaves in a similar manner.

It is the failure of this adjusting mechanism which marks off the toxemias from the normal.

TABLE III. SHOWING APPROXIMATE WATER AND SALT BALANCES ON LOW AND HIGH SALT DIETS IN NORMAL PREGNANCY

WATER INTAKE c.c.	URINE OUTPUT c.c.	APPROX. NACL INTAKE gm.	CL OUTPUT AS NACL. gm.		BLOOD ANALYSIS	
					NACL	SERUM PROTEIN
Carbohydrate Diet						
1202	1508	3	3.77	Last 3		
1302	1228	3	3.68	days of	mg. per	per cent
1300	1225	3	3.33	salt-poor	100 c.c.	
3804	4163	9	10.78	diet	479	5.97
Balance -359		Balance -1.78				
1240	840	+15	7.64	First 3		
1140	946	+15	11.35	days of		
1280	902	+15	10.95	salt-rich		
3560	2688	+45	29.94	diet	489	4.76
Balance +872		Balance +15.06				
Protein Diet						
1230	972	3	3.88	Last 3		
1230	1360	3	4.21	days of		
1130	771	3	3.54	salt-poor		
3590	3103	9	11.63	diet	472	6.21
Balance +487		Balance -2.63				
1670	820	+15	7.45	First 3		
1430	990	+15	12.84	days of		
1510	1018	+15	15.34	salt-rich		
4610	2828	+45	35.63	diet	508	5.53
Balance +1782		Balance +9.37				

CASE 1.—Aged forty-two, para vii, nine months, headache, edema, albuminuria, blood pressure 150/108. Previous pregnancies marked by similar symptoms. Five living children.

The case might be classified as a recurrent toxemia or a low reserve kidney. On milk and orange juice, or on a carbohydrate salt-poor diet the clinical symptoms

rapidly ameliorated. Nine days after admission 15 gm. of salt were added to the carbohydrate diet. Within four days all *the original symptoms returned together with blurring of vision*. Two days after discontinuance of the high salt intake the patient went into labor.

CASE 2.—Aged thirty-two, para v, eight months, edema, and blurring of vision. No albuminuria or rise in blood pressure. Disappearance of symptoms on high protein diet with 3 gm. salt. *Return of edema and general dull heavy feeling on ordinary hospital diet*. Normal labor. Baby weighed 4 pounds 4 ounces. Pregnancies 1 and 3 had been marked by preeclamptic symptoms followed by convulsions.

CASE 3.—Aged twenty-two, para i. Had been on high protein and high fat diets as a normal pregnancy. *Developed marked edema on ordinary hospital diet on 2 occasions*. No other symptoms. Salt-poor protein or fat diet caused disappearance of edema. Normal labor. Baby weighed 4 pounds 8 ounces.

CASE 4.—Aged twenty-four, para ii, seven and one-half months. Admitted with headache, blurring of vision, edema, albuminuria, blood pressure 210/140. Placed on mixed diet salt-poor for nineteen days. Edema almost entirely disappeared. Blood pressure 120/70. Given 30 grams sodium bicarbonate daily with same diet. *Edema returned in three days and blood pressure rose to 176/80 in seven days*. Edema and blood pressure subsided in a week on discontinuance of sodium bicarbonate. A 6 pound macerated fetus delivered 13 days later.

In view of our observations we felt justified in concluding that neither protein nor fat was the causative dietetic agent of toxemia of pregnancy. The action of the sodium salts in causing disturbances however had to be preceded, or accompanied by, some change in the pregnant organism. The normal pregnant woman could resist and set herself at equilibrium at varying levels of salt intake. Whether there is any level at which in the normal, the resistance breaks down and she becomes a toxemic, and whether that possible level is lower than in the nonpregnant condition, we do not know. An intake of 15 gm. of sodium chloride is a high intake. To accomplish this we had to administer part in gelatin capsules. Baird and Haldane<sup>10</sup> observed visible edema in normal man after 35 to 40 gm. salt intake in one day.

We next made observations on the use of hypertonic saline solutions. In other conditions they have been used to relieve intracranial pressure. Would they be of use in eclampsia? According to our previous observations—No! No conclusion in medicine is valid however for all cases and under all conditions. The variation in biologic factors is too great. The arguments pro and con have been set forth in a previous paper.<sup>11</sup> We accordingly gave 300 c.c. of 10 per cent sodium chloride solution to 4 subjects, giving the solution very slowly between the hour of 9 and 11 A.M. A little cracked ice was allowed to allay thirst.

CASE 1.—Normal. Hypertonic saline showed no alteration in any characteristic pointing to a toxemia. A second injection on the following day produced diarrhea but no other signs of disturbance (Chart I).

CASE 2.—Doubtful toxemia. Admitted with slight rise in blood pressure which fell at once on rest in bed with salt-poor diet. The hypertonic saline produced gastric disturbance and headache on the day of the administration. The blood pressure fell to a slightly lower level (Chart I).

CASE 3.—Mild toxemia. This patient had been followed carefully in special clinic, as previous pregnancy had shown toxemia with loss of fetus. Weight changes during pregnancy were irregular. Albuminuria developed and slightly increased blood pressure. Saline was given intravenously morning after admission. Blood pressure, both systolic and diastolic and albuminuria, increased next morning. Epigastric pain, with nausea and vomiting for remainder of day. Headaches for two days. Labor in three days. Living baby (Chart II).

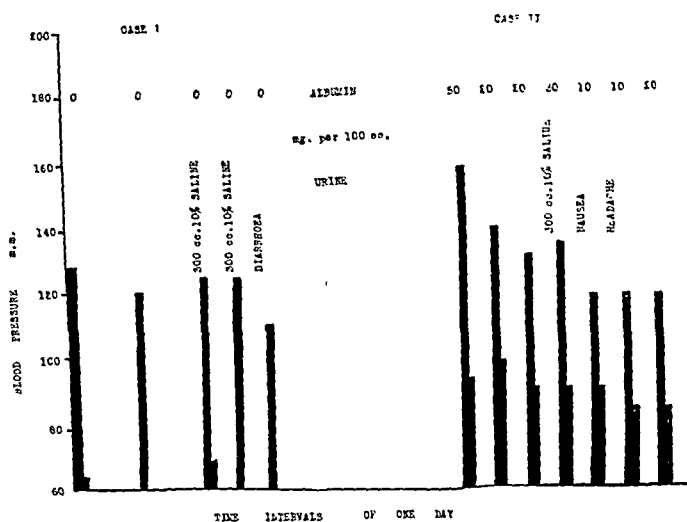


Chart I.—Showing effect of hypertonic saline in normal pregnancy and doubtful toxemia. Columns show systolic and diastolic blood pressure.

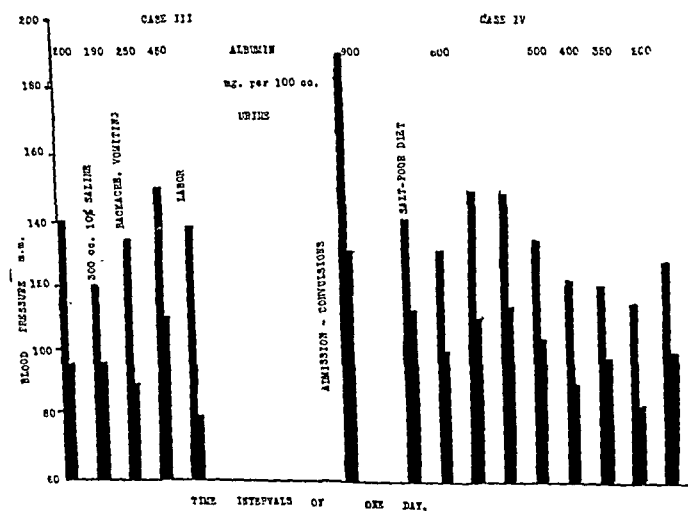


Chart II.—Showing systolic and diastolic blood pressures, etc., in toxemias.

CASE 4.—Eclampsia. Primipara, nine months. Record of 1 convulsion before admission. High blood pressure and albuminuria. No edema. No evidence of liver disturbance. Morphine and gastric lavage on admission. No further convulsions. Placed on mixed ordinary salt-poor diet. Observed for seven days, during which time blood pressure and albuminuria decreased (Chart II). On the eighth day, 18 gm. of NaCl in 300 c.c. of water were given intravenously. Systolic and diastolic blood pressure raised in evening and also next morning. On the ninth day, 30 gm. of NaCl in 300 c.c. of water were given intravenously. Headache, epigastric pain, vomiting almost immediately. Rapid rise in blood pressure throughout the day.



Oliguria. Convulsions at 9:30 P.M. Labor. Baby born at 10:30 P.M. Large amount of fluid from bowel during labor. The nonprotein nitrogen rose from 43 to 60 mg. and the  $\text{CO}_2$  combining power dropped from 38 to 29 vols. per cent.<sup>12</sup> Increased albuminuria in next morning's urine. Uneventful puerperium (Chart III).

Again the administration of salt has given no sign of toxemia in the normal pregnant woman, but has intensified or revived the symptoms in the already toxemic. The results in the last case were so dramatic and followed so swiftly on the heels of the injection that we feel we dare not continue our observations in this direction. *The dietetic factor in the production of a toxemia of later pregnancy is neither protein nor fat, but salt.* This is not a new view. Lafont<sup>13</sup> expressed the same view years ago as a result of clinical observation on the difference in the incidence of eclampsia in the European and native population of Algiers.

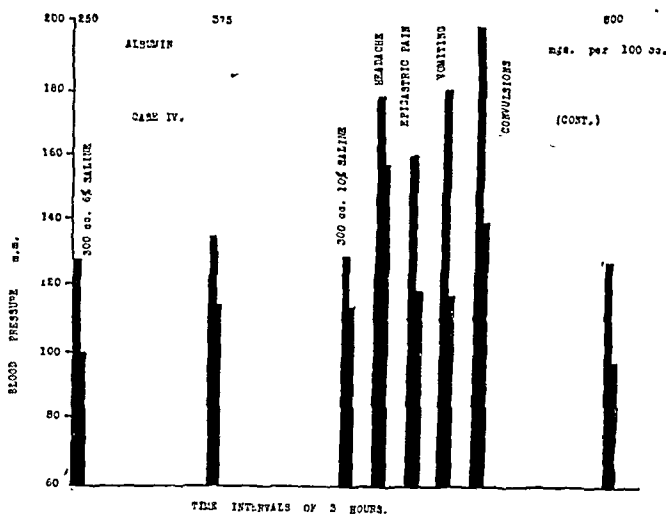


Chart III.—Showing action of hypertonic saline on recovering eclampsia. Columns show systolic and diastolic blood pressure.

All of these 4 women showed a common symptom after the hypertonic saline, a disturbance of the gastrointestinal tract. In the strictly normal pregnancy this took the form of diarrhea, but in the other three, epigastric pain and vomiting. In Case 4 there was a violent outpouring of fluid from the bowel during labor. No analyses of the fluids were made, but it does not seem unreasonable to suppose that the body made an effort to get rid of the excess of sodium by the gastrointestinal route. The gastrointestinal fluids contain considerable quantities of base, consisting chiefly of sodium.<sup>14</sup> Such observations permit us to speculate on the origin of many of those attacks of "acute indigestion" in pregnancy which may usher in eclampsia itself. Do they represent the violent effort to get rid of an excess of base by the gastrointestinal tract, and if so what forces are at work which have brought about the necessity in an apparently normal pregnant woman? The nausea and vomiting of late pregnancy may have its origin in some similar salt and water disturbance.

It is impossible in our present state of knowledge to separate the relationship of sodium salts and water. If sodium salts are retained so is water, even to the point of edema. Are all the symptoms of toxemias of late pregnancy to be explained on a theory of water and sodium retention, a retention resisted successfully by the normal but not by the abnormal pregnancy, and whose abnormality we recognize under the general heading of toxemia? Such a view is akin to the old view of Traube and Rosenstein<sup>15</sup> revived in a more modern form by Zange-meister.<sup>16</sup> Does a study of some of the suggested forms of therapy reveal any such indication?

#### TREATMENT

In discussing the different forms of treatment we have no intention of contributing to that perennial discussion, radical or conservative measures. Our discussion is limited to types of therapy which seem to have a relationship to the possible action of sodium salts or changes in the water balance.

##### A. SPECIAL THERAPEUTIC MEASURES

(a) *Venesection*.—This old method of treatment is now in little use. Those who offer any defense at the present day consider it only of use if a large amount of blood is removed. It would be under the condition of a large venesection that the procedure would be of most value in removing both sodium salts and water. The variation of Irving and Taylor,<sup>17</sup> in which the corpuscles are replaced in the patient might perhaps be improved by using isotonic glucose solution instead of normal saline.

(b) *Purgation*.—Under ordinary conditions the loss of water and sodium salts by the bowel is very small. Under conditions of diarrhea the loss may be considerable. Magnesium sulphate is to be preferred, at present, though we should like to see observations on the use of potassium acid phosphate.

(c) *Sweating*.—The use of hot packs, etc., has been almost entirely discontinued. Yet profuse sweating will remove moderate amounts of water and sodium salts. The procedure of hot packs however, is troublesome and is somewhat disturbing to the patient, whereas importance of administering treatment without disturbance is a recognized essential. The results obtained are usually not commensurate with the effort, yet we believe modern hydro- or electro-therapy might develop conditions, which would be of service in some cases.

(d) *Intravenous Magnesium Sulphate*.—Lazard and others<sup>18</sup> have reported enthusiastically on the use of this compound. There are evidently limitations to its use however.<sup>19</sup> In our opinion its success is due to the diuretic effect of the  $\text{SO}_4$  ion, and the sedative action of the Mg. ion.

(e) *Intravenous Glucose*.—Titus<sup>20</sup> for some time has advocated the use of hypertonic glucose solutions given intravenously. His original reason was to maintain the liver at as high a glycogen content as possible. More recently he has claimed a relative hypoglycemia as an actual cause for the convulsions. Quite apart from the controversy on his assumptions and biochemical findings, the giving of glucose in large and sudden quantities produces changes other than in the carbohydrate metabolism. It is these changes which may be helpful. One of us in experimenting with doses of glucose at different times of the day has noticed the production of an anuria followed by a profuse diuresis following its use. The period of anuria was accompanied

by a marked dryness of the skin. We interpret this as a shift of water from the peripheral vessels to the central areas, which water afterwards becomes available for the production of urine. The anuria which can be produced in this way has been previously noted in rabbits.<sup>21</sup> The use of insulin combined with glucose to combat the acidosis of eclampsia was advocated by Stander and Duncan, etc.<sup>22</sup> The addition of insulin to the glucose may ensure the same changes with small amounts of glucose, which Titus obtains with the more concentrated solutions.

(f) *Ammonium Chloride*.—This was recommended by Mussey<sup>23</sup> in a dose of 10 gm. a day. It has a well-known diuretic effect on account of its acid producing properties. It will reduce edema, but Mussey is of the opinion that the changes brought about by the ammonium chloride extend beyond the simple reduction of edema. Other ammonium salts might be of use. The chloride is difficult to administer on account of its unpalatability. Harding and Silverthorne<sup>24</sup> showed that ammonium acid phosphate in large doses produced lowering of the CO<sub>2</sub> combining power of dogs similar to that produced by ammonium chloride. Scott<sup>25</sup> recommends the phosphate for the production of acid urines in the treatment of pyelitis, stating the unpalatability of this salt is much more easily disguised. As in the use of ammonium chloride, observations on the CO<sub>2</sub> combining power would be necessary to make sure that too large a dose of phosphate is not given. We feel however, any rise in the blood urea need not produce alarm. Indeed a raised blood urea may be helpful in maintaining diuresis.

#### B. NUTRITIONAL THERAPEUTIC MEASURES

(a) *Milk*.—The use of milk inevitably means the use of a low calorie medium-protein sodium-poor diet. How far beneath the calorie requirements of the woman the milk diet may fall, depends upon more than one factor. A liter of milk contains 35 gm. protein, 50 gm. carbohydrate, and 35 gm. fat. Its calorie value is 655. Two liters of milk a day would be the maximal amount which any average sized woman could take. Indeed from 1200 to 1500 c.c. would be a considerable intake, a calorie value of 900 to 1300. This would be considerably under the calorie requirements of all but the very smallest of women. Only our fat diet No. 2 approximates this in calorie value. The calorie requirements of a woman during pregnancy are variable. In general they increase per kg. of body weight as pregnancy progresses. As a general calculation the nonpregnant woman in bed would require 28 calories per kg. per day as a basal diet. It would be underestimating the resting calorie requirements of the pregnant woman at 30 calories per kg. per day. A 60 kg. (132 pound) woman would thus require 1800 calories. Thus practically all women are undernourished on a milk diet.

(b) *Starvation*.—This is part of the treatment as advocated by the Dublin School.

(c) *Starvation and Water Deprivation*.—This, carried out over a period of three days, has recently been advocated by Seitz<sup>26</sup> and by Baumgart<sup>27</sup> for severe toxemias. It is in conformity with some of the methods of treatment of nephritis. It is im-

TABLE IV. GERMAN WAR DIET

	GRAMS	PROTEIN	CALORIES
Bread	271	17.2	688
Potatoes	357	7.5	341
Butter and Margarine	11.4	—	89
Meat	36	4.5	78
Eggs	—	1.0	13
Sugar	26	—	104
Cereals	9.8	0.9	31
Totals		31.1	1344

portant because it represents a conscious effort to rid the body of cellular water as well as edema fluid. The restriction is unquestionably irksome, but in actual eclampsia is probably not so irksome as it sounds, on account of the semicomatose condition during part of the time. The treatment of a potential eclamptic by this method, who feels well and who perhaps is barely persuaded of the gravity of her position, would be difficult.

(d) *The "War Diets" of the Central European Empires.*—The war diets fell far short of the amounts planned by the German and Austrian physiologists. They were low in protein and fat, but how inadequate they were in calories is not so generally known. The rationed diet, as actually supplied is shown in Table IV.<sup>28</sup> In caloric value it is at least as low as the milk diet used in preeclamptic therapy.

(e) *Salt-poor Diets.*—These have already been discussed.

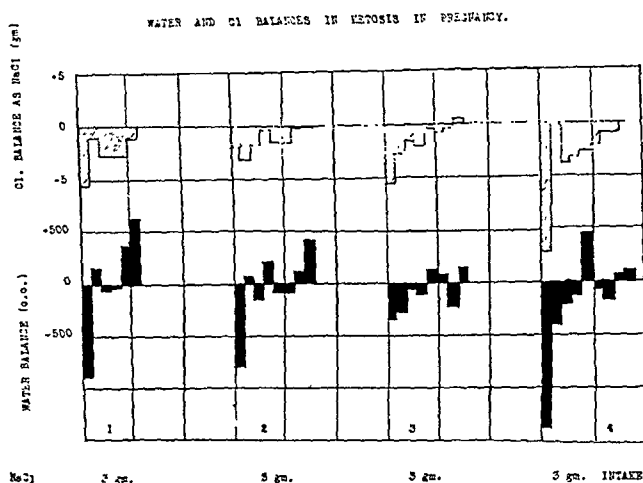


Chart IV.—Showing water and Cl balances in normal pregnancy on salt-poor ketone-producing diets. Previous diet of subjects 1, 2, 3 was salt-poor. Previous diet of Subject 4 was salt ad lib.

In the foregoing résumé of some therapeutic measure we have shown that many either consciously or unconsciously remove water, and thus sodium salts. Common to all the diets we have mentioned is the factor of undernutrition, sometimes moderate, sometimes severe. Is the undernutrition as valuable as the absence of salt? Is eclampsia to be regarded, partially, perhaps as a disease of overnutrition or plethora? If so the ideas with which this work was commenced may require some revision. In presence of severe undernutrition the possibility of another factor enters into our discussion, the production of ketosis and the removal of cellular water. In the starvation treatment of Tweedy, Seitz, Baumgart, etc., ketosis must certainly be present. It is well known, especially since the work of Gamble, Tisdall and Ross<sup>29</sup> that in presence of the ketosis of starvation, water leaves the cells of the body. A change in the water balance is also noticed in diets high in fat. Benedict and Milner<sup>30</sup> showed that losses of body water occurred, when the 67 per cent of the caloric needs were derived from fat. This point is certainly reached in many of the undernutrition diets we have been mentioning. Harding, Allin, Eagles and Van Wyck<sup>31</sup> noticed losses of water on the first

day of a high fat diet in normal pregnancy even if the previous diet had been salt-poor. If the sodium chloride intake is kept low and constant, there is also to be noted a continuous negative chloride balance (Charts IV and V). The balance changes when the low sodium chloride intake is changed to a high intake. These observations would support the idea that a certain degree of ketosis might be beneficial.

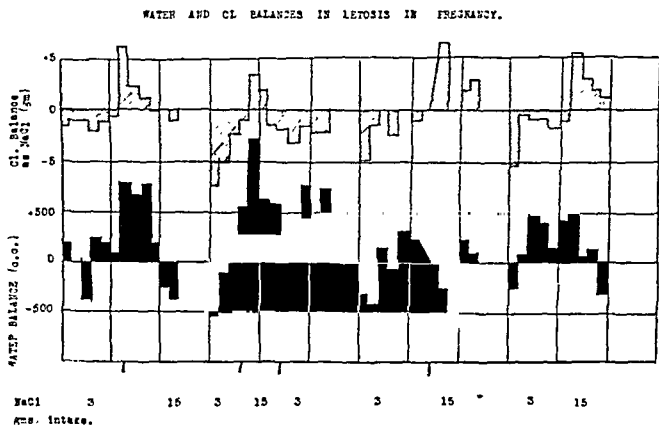


Chart V.—Showing water and Cl balances in normal pregnancy on ketone-producing diets, with alternations in intake of sodium chloride.

It is interesting to notice at this point the analogy which has developed between the partial etiology of epilepsy and eclampsia. Ketone-producing diets are claimed to be beneficial under controlled conditions in the treatment of epilepsy.<sup>32</sup>

We have not made any prolonged observations on the effect of ketone-producing low salt diets on the toxemias of later pregnancy. We have shown that they are harmless in normal pregnancy. One of our diets is of very simple composition, is naturally almost salt-free and is liquid, thus allowing easy control.

Calories 1546	Cream (32%)	320 gm.	Protein	40 gm.
	Whole Milk	670 gm.	Carbohydrate	45 gm.
	Egg White	85 gm.	Fat	129 gm.

Such a mixture can be given in small quantities throughout the day to any desired amount.

A possible criticism will present itself. A ketone-producing diet will often lower the level of the plasma bicarbonate. The plasma bicarbonate in actual eclampsia is sometimes at acidosis level. Obviously care should be maintained under those conditions. Observations in our own laboratory (unpublished) have shown us that large doses of urea will raise temporarily the CO<sub>2</sub> combining power of the plasma. Urea is also a powerful diuretic. It is harmless in a normal pregnancy and in a mild toxemia, according to our few observations. It has been used in the treatment of epilepsy in combination with ketone-producing diets by McQuarrie,<sup>32</sup> Maclean,<sup>33</sup> Crawford and McIntosh<sup>34</sup> and Feilchenfeld<sup>35</sup>

have administered it freely in nephrosis. There is thus no reason against its use. We should recommend a dose of 60 grams urea and 10 grams of citric acid in 10 per cent solution in 10 divided doses per day. The presence of the citric acid makes the urea solution more palatable.

The suggested use of high fat diets would probably be better applicable to thin or moderately nourished women. Heavy, overweight women would probably be benefited more by severer restrictions.

#### WEIGHT CHANGES IN RELATION TO THE TOXEMIAS

The series of observations in the preceding sections can be interpreted as favoring Zangemeister's theory. In its later form, "hydrops gravidarum," he attempts to explain the symptoms as a form of edema. One important feature of Zangemeister's ideas is the possibility of recognition of a toxemia of later pregnancy by following the weight changes of the patient. Abnormal gains in weight are an index of an oncoming toxemia. Observation of the weight of the patient is well known as a clinical test of impending edema in other diseases. Confirmation of this part of Zangemeister's views has come from many quarters. Moreover water retention evidently plays a part, or at least accompanies, toxemic signs other than edema. De Wesselow and Wyatt note "in some apparently nonedematous cases of eclampsia water may therefore be present in spite of the clinical findings." This observation was made as a result of their study of water balances in the puerperium.

If there is so much evidence in support of Zangemeister's view, why has it not gained more general acceptance? We know many prenatal clinics where no record is kept of the patient's weight. The somewhat casual attendance of ignorant patients at an outdoor clinic certainly militates against the correct collection of data of this kind, but even in many private practices where conditions are favorable, the use of scales and the charting of weights is by no means universal.

Increases in weight during pregnancy are variable, depending on many factors; age, dietetic habits, exercise, presence of infection as well as variations in the general tendency to put on weight during pregnancy. The general gain in weight varies from  $3\frac{1}{2}$  to 5 pounds a month. Kerwin's<sup>36</sup> average figure for 127 pregnancies is 2 pounds a month in the latter half of pregnancy. Davis<sup>37</sup> has stated that a gain per month of 7 to  $7\frac{1}{2}$  pounds or over is pathologic in character. Bingham<sup>38</sup> has recently stated that gains of over 4 pounds a month are to be considered abnormal. There is evidently a wide variation in opinion on normal standards. Our records of three normal pregnancies and one toxemia are shown in Chart VI. At a glance it is impossible to distinguish the normal from the toxemia. Both Subject III and Subject L show monthly gains of over 7 pounds. Nor do the fortnightly records show up any essential difference. Indeed of the two it is the normal pregnancy which shows more consistently the large gains. Zangemeister's

views may enable the obstetrician to distinguish the preedematous stage of a grossly water-logged toxemia, but it apparently fails to warn him of a toxemia such as is present in Subject III, if Subject L is to be considered normal. Yet Subject III was one of the patients whose albuminuria and blood pressure was increased by the hypertonic saline

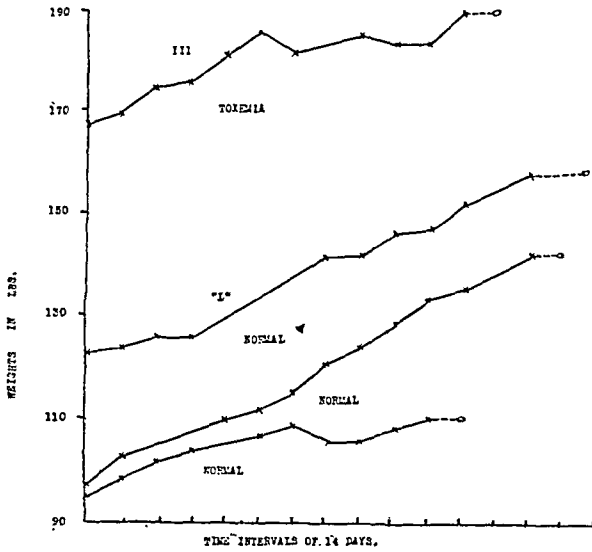


Chart VI.—Showing weight changes during pregnancy.

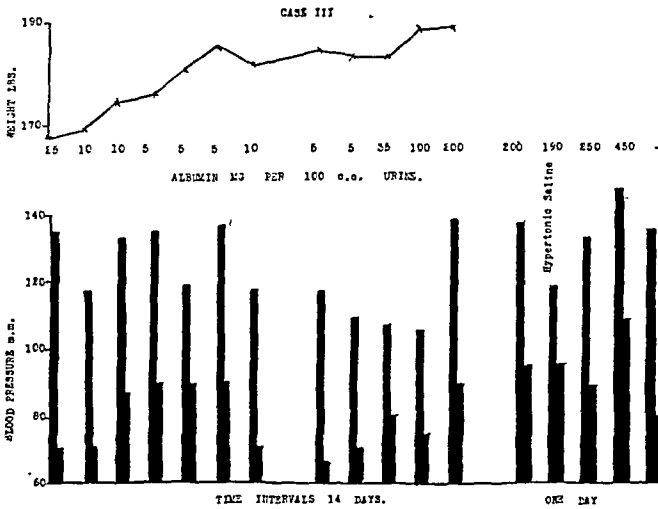


Chart VII.—Showing development of toxemia under ordinary conditions and its exaggeration by hypertonic saline.

treatment. Fundamentally this case should be an example of water retention, but before dismissing Zangemeister's ideas entirely, let us examine the collected data as shown in Chart VII, a little more closely.

The first 5 recorded weights show a period of active gain, with a normal content of albumin in the urine and a fluctuating blood pressure, which just fails on 4 occasions to reach the accepted danger point of

140 mm. Next, the weight is practically stationary with a markedly decreasing blood pressure. There is a normal albuminuria until ten weeks after the highest recorded weight. Then albumin appears in the urine in an amount just over the normal limit. In the next fortnight there has been a gain in weight and now the albumin is marked. A week later the blood pressure has risen to 140 mm. and the albuminuria has further increased. Note that the developing toxemia is now showing itself in the kidney rather than in the blood pressure. It was at this point that the patient was brought into the hospital. Can we interpret the weight changes in accordance with the development of the toxemic symptoms? The period of approximately constant weight was not marked by an infection, a common source of loss of weight of which an example is shown in one of the "normal" curves. The period of constant weight may be interpreted as a balance between the normal weight gains of pregnancy and a loss of fluid accumulated in the fore period. The loss of fluid lowers the extravascular pressure and the blood pressure falls. The toxemia, however, has been initiated and shows itself at the patient's weakest point, the kidneys. Such might be one interpretation. Ten weeks however have elapsed since the end of the period of rapid weight gain. This seems a long time to wait for evidence of the kidney disturbance, especially when other signs point to improvement. It seems more probable to us that in addition to general gains in water, local gains in water can be made by the different organs. These excessive local gains may be made even when the weight chart shows only the normal increases, or in such a subject, as this, no increase at all. If such be the interpretation it renders impossible the early detection of every toxemia by a study of weight charts. Only those cases can be detected of which one of the symptoms is a generalized water retention. Whether a generalized retention of water always precedes or accompanies the localized disturbance, we have no evidence.

Of intense interest to us is the evident connection between the toxemia, as it developed naturally in this patient and its exaggeration as seen in hospital under the influence of the hypertonic saline. We have just pointed out how, after some slight increase in blood pressure, which subsided, the toxemia developed suddenly in the kidney. The disturbance affected the blood pressure to a lesser degree than the kidney. After the hypertonic saline, the blood pressure increased, unmistakably, but the major effect was the increase in the albuminuria. *The action of the hypertonic saline was to exaggerate the toxemia in the direction in which it was proceeding under natural conditions.*

That such small localized changes in water distribution affecting single organs rather than the whole vascular system can occur is rendered more probable when we find that rapid shifts in water can be observed occurring over the whole body. We published in another paper an account of an unusual fluctuation of symptoms in a toxemia occur-



ring in one of our colleague's patients. In the presence of a generalized edema, the blood pressure fell. When in the space of twenty-four to forty-eight hours the edema subsided, the blood pressure rose to the point of convulsions.

Zangemeister's ideas therefore need not be discarded, but we believe they require modification. The excessive gain in weight may affect the whole body, but it may also be localized, perhaps without any such general weight increase. Following the preedematous stage in any one organ, comes hemorrhage and necrosis, such as is recognized at autopsy. The theory requires modification to allow for changes in the *internal* distribution of water, as well as changes brought about by *external* agencies. Such a view allows the possibility of a common origin to the usual toxemic disturbances, and also to anemias of pregnancy, accidental hemorrhage and the development of true diabetes in pregnancy.

We have attempted to interpret the toxemias of pregnancy in terms of a water or sodium balance. We recognize that even if our interpretation is true, it only represents one phase of a complex problem.

#### CONCLUSIONS

1. Observations on the effect of added salt to the diet, or on the use of hypertonic saline solutions show, that the normal pregnancy remains normal, and that the toxemic pregnancy has an exaggeration of symptoms.

2. A study of many of the older and some of the more recently suggested forms of treatment shows that they cause the removal of water from the body, or may be involved in some change in the internal distribution of water.

3. The "edema" theory of Zangemeister, at present, offers the most unifying view of the toxemias of later pregnancy. It requires modification, however, to allow for the formation of edema in individual organs, apart from a generalized water retention, and for the possibility of internal changes in water distribution.

4. Further progress might be made by a more intensive study of the atypical forms of toxemia and by a wider acceptance both in theory and in practice of the value of observations of weight during pregnancy.

5. The variability of the toxemias of later pregnancy is in harmony with the assumption that they possess one origin and a multiplicity of symptoms.

The authors wish to express their indebtedness to the Medical Research Committee of the University of Toronto for assistance during the progress of these researches.

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(For discussion, see page 945.)

Mgalobeli, M.: The Influence of Employment in Tobacco Factories on the Reproductive Organs of Women. Monatschr. f. Geburtsh. u. Gynäk. 88: 237, 1931.

Tobacco is a poison and affects the gonads. The social surroundings, however, are also important. In the large series of cases studied by the author an equal number of abnormalities was found in those who stood up during their work and those who sat down. Menstrual disturbances were very common. The more the women came into contact with tobacco dust and the worse the home surroundings, the more leucorrhoeal discharge they had. The number of pregnancies and labors were diminished and there was an increase in the frequency of spontaneous abortions and deaths of children from one to three years of age. All of these conditions are definitely attributable to the direct or indirect effect of nicotine on the sex organs. The author urges that girls up to the age of 18 should not be permitted to work in tobacco factories. Furthermore women employed in such factories should not be permitted to remain in any one position during work for a long time. There should be frequent periods of rest and where possible these should be combined with compulsory gymnastic activities. To avoid direct irritation of the genitalia the author advises that the women workers wear proper undergarments.

J. P. GREENHILL.

## THE RELATION OF THE ANTERIOR LOBE OF THE HYPOPHYSIS TO GENITAL FUNCTION\*

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I CONSIDER it an honor to be asked to speak on my hormone studies before an American audience, because of the outstanding discoveries which have been made in the United States in this field of research. Without American investigators the modern study of the sexual hormones would have been impossible. May I be permitted to mention but a few of those whose work was of great importance to me, namely Leo Loeb, Robert T. Frank, Evans, P. E. Smith, Stockard and Papanicolaou, Long and Evans, Allen and Doisy, Engle, and Corner.

Within the limited time given, I can speak only of those of my researches and their results made within the last few years.

Having succeeded in preparing an aqueous extract of ovarian hormones (folliculin), I found that with it the estrus could be produced in infantile animals but notwithstanding this artificially procured sexual prematurity, the ovaries themselves remained unaffected. The impulse which starts ovarian activity does not originate in the ovary but somewhere else, namely, as I discovered, in the anterior lobe of the hypophysis. I shall not dwell on the details of these studies but desire to state merely my final conclusion, namely, that the anterior hypophyseal lobe is the motor impulse for sexual function. Its hormones represent the superimposed, nonspecific, general, sexual hormones. The hypophyseal hormones are primary, the specific sexual hormones are secondary factors.

Introduction of anterior hypophyseal substance in the infantile rodent results in three morphologic and functional effects: HVR I = ripening of follicle and start of estrus, HVR II = hemorrhages in enlarged follicles ("blood points"), and HVR III = formation of corpora lutea,—luteinization. The practical importance of these effects lies in the fact that these three specific reactions are available as an exact test (Zondek-Aschheim) for the presence of anterior hypophyseal hormones and thus have made it possible to study the relation of the anterior hypophyseal lobe to the organisms. By means of this test I succeeded in developing a chemical isolation of the anterior lobe hormone, to which I gave the name "Prolan." In comparison with folliculin, prolان is a sensitive substance which is destroyed by a temperature over 60° C. It can be produced in sufficient purity to render it available for clinical use. However, I shall not speak of clinical problems, and refer the interested reader to my book,

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\*Read, by invitation, at the Fifty-Seventh Annual Meeting of the American Gynecological Society, Quebec, Can., May 30 to June 1, 1932.

*Die Hormone des Ovariums und des Hypophysen-Vorderlappens.* (Berlin, Springer, 1931.)

Of late the chemic identity of the prolan produced by the hypophysis and that extracted from the urine of pregnant women has been questioned, though both yield the typical reactions HVR I to III. While Evans, in hypophysectomized rats, observed an ovarian effect decidedly more marked with anterior lobe extract than with pregnancy urine, Hill and Parkes, in hypophysectomized rabbits, failed to notice any difference. Most interesting is Evans' observation that the hypophyseal growth hormone intensifies prolan reactions; a fact which points to a close interrelation between these hormones. It seems that the definite answer in regard to chemic identity of lobe and urine extracts will not be forthcoming until both these substances will be available in chemically pure form.

Chemical analysis likewise will solve another problem; whether prolan is a single hormone or a mixture of two, as we assume from biologic effects, namely, a hormone "A" causing ripening of follicles, and a hormone "B" causing luteinization. It is possible that we are dealing with different isomeres of the same molecule. Assumption of a duality of prolans explains to us also why the ovary produces hormones, the one of the follicle and the other of the corpus luteum. Thus hormone A (the folliculation hormone) would be the controlling sexual hormone which, through folliculin, leads to the proliferation phase, while the luteinizing hormone B through the contained progestin, starts the functional phase and later exerts a protecting influence over the implanted ovum.

Objections have been raised to our conception (Zondek and Aschheim) of the anterior lobe as the activating motor for sexual function. Some investigators assigned to the maturing ovum supremacy in the generative process, others vested it in the corpus luteum. Without doubt, as I emphasized in my book, the anterior lobe of the hypophysis is influenced also by ovarian hormones, so that folliculin might stimulate or retard the output of anterior lobe hormones. However, in view of the mutual interdependence of all endocrine glands and of the fine gradation of their chemic output, it is not surprising that interrelations between these glands are manifold as well as intimate. As I have expressed it, the motor of sexual function is regulated also by its own products. Nevertheless, the fact remains that the anterior lobe exerts superior authority over the genital sphere. This can be deduced, e. g., from the following experiments: Removal of the hypophysis ends all functional activity of the sex gland. Without a hypophysis, there is no follicle maturation, no impregnation. If, on the other hand, the sex gland is removed, the anterior hypophyseal lobe not only keeps on functioning but, indeed, puts out more prolan. With prolan, as previously shown, we can initiate every phase of the genera-

tive cycle. The follicle is made to mature and to rupture. The liberated ova migrate through the tubes into the uterus (Figs. 1 and 2). In collaboration with Boeters I succeeded even in the fertilization of such ova in an infantile animal and thus a pregnancy was produced in an infantile rat by means of prolan (Fig. 3). With prolan we were able also to induce follicle maturation and liberation of ova even in the pregnant animal and thus to annihilate the generally accepted law of ovarian dormancy during pregnancy. By means of prolan in senile animals the quiescent ovarian activity can be restored with rhythmic return of the estrus. All these

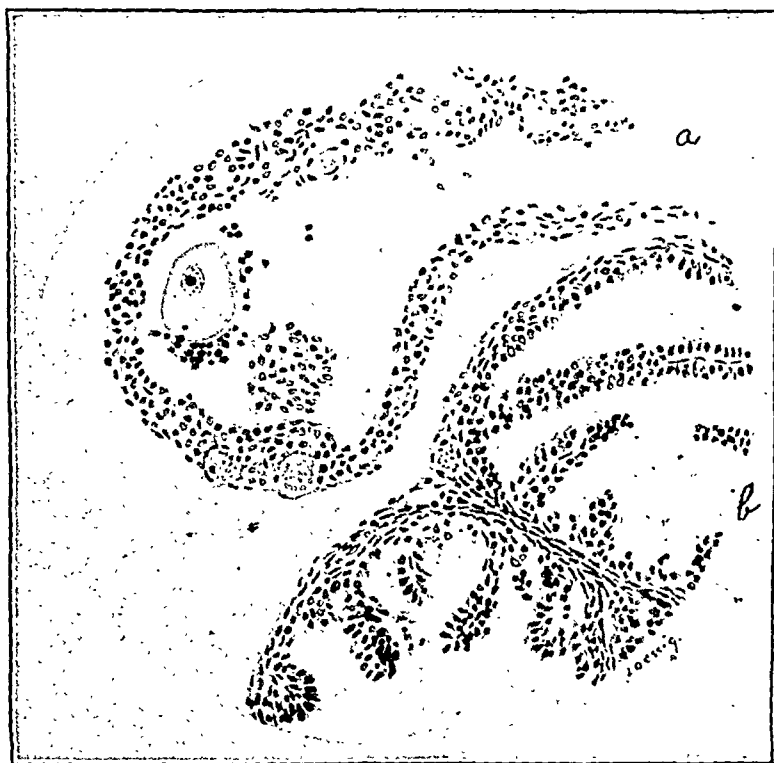


Fig. 1.—Section of tube from an infantile mouse after treatment with prolan (a) fimbria, (b) tube. The artificially liberated ovum in the fimbria.

facts, established in experiments, seem to support our contention of the supremacy of the anterior lobe over the sex gland.

With some certainty we can designate in the anterior lobe the part producing the prolan. It is elaborated by the basophilic cells, as proved in the following experiment: I implanted posterior lobe of the hypophysis of the human being and of cattle into infantile mice. The head part of the posterior lobe fails to cause HVR I to III. On the other hand, that part of the posterior lobe which is immediately adjacent to the anterior lobe contains prolan only in the human being and not in cattle. As demonstrated by Berblinger, in the human being but not in cattle, cell strands run from the anterior into the posterior

lobe, these strands consisting entirely of basophilic cells. This, in my opinion, justifies the deduction that in the human being it is the basophilic cells which produce prolan. Evans and Simpson, also Berblinger, after various experiments also arrived at the conclusion that the basophilic

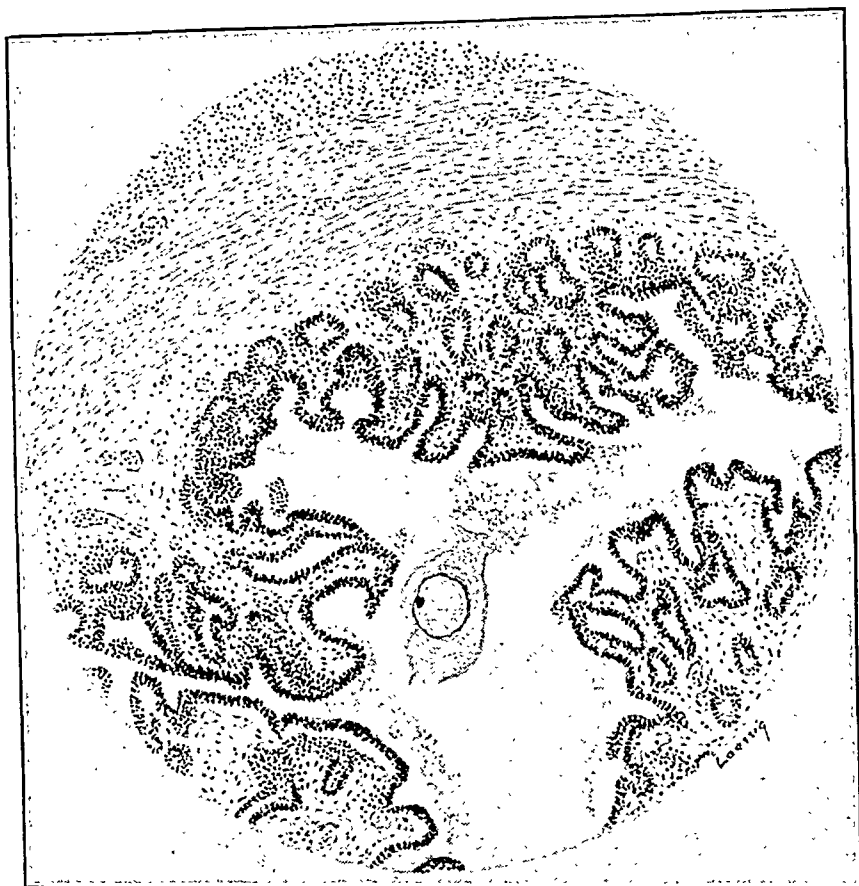


Fig. 2.—Section of infantile rabbit uterus after treatment with prolan. The artificially liberated ovum in the uterine cavity.

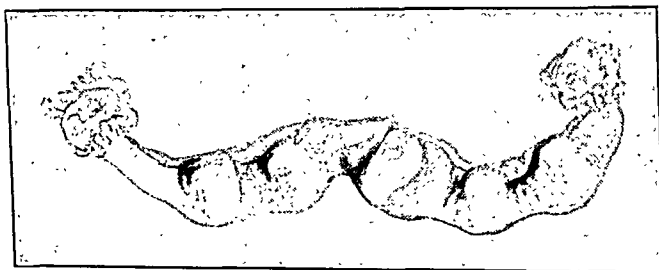


Fig. 3.—Genital organs of infantile rat after treatment with prolan and fertilization. Six embryos in the uterus.

cells in the anterior lobe furnish the prolan, though according to Kraus the eosinophilic cells likewise possess this faculty.

Prolan exerts an effect also on the male sex apparatus. But this effect, as shown likewise by P. E. Smith, Steinach and Kun, Borst, Doederlein and Gostimirovic, is not as characteristic in the male as it is in the female.

We might obtain with prolan some enlargement of the testicles and marked proliferation of the prostate and particularly of the seminal vesicles, even spermatogenesis may seem to be stimulated in infantile animals, but it is impossible to achieve prematurely, full maturation of spermia. With an increase of the dose of prolan, the enlargement of the testicles can be augmented, but this is the result solely of hypertrophy of the interstitial tissue and not of the generative tissues. Both in woman and in man, this prolan effect reaches the sexual organs solely by way of the sexual gland. Prolan exhibits no effect in the castrated buck. From investigations carried out with Boeters we conclude that hormone A influences the generative and hormone B the interstitial apparatus together with the adjunct organs of the testicle.

Reactions HVR II and III form the basis for the hormonal pregnancy test made with urine. Since this method is well known in America, further remarks would be superfluous. It is indeed a method for early diagnosis, because it is found to be positive within five or six days after nonappearance of the expected menstrual flow. Reports from the literature of the world prove that the test is correct in about 98 to 99 per cent, which probably represents the optimum for any biologic method. Two objections to the method have been advanced: (1) some urines are too toxic to be injected, amounting to approximately 6 to 7 per cent of all specimens; (2) the test takes four days. These disadvantages I eliminated by extracting the toxic substances with ether and adding a 3 per cent solution of dextrose. This procedure makes all urines available for the test and also reduces the time for reactions from four to three days. I desire to call attention to a recent improvement in technique. If I am not quite certain whether the ovary of the injected infantile mouse contains a "Blutpunkt," or hemorrhagic spot, I remove it and after washing in water place it in glycerin. In this manner the tissue clears up and the spots, when present, become visible through the contrast in color. In case of doubt, a corpus luteum can be made visible in the excised ovary by squeezing it between two glass slides. The follicles under pressure appear as spherical clear spaces, the corpora lutea as darker and larger formations. In looking on them under the microscope the diaphragm should be almost closed.

A noteworthy modification of the Aschheim-Zondek pregnancy test here in America has been introduced by Friedman and Schneider. They inject the urine not subcutaneously into mice but intravenously into rabbits. The time required for the test is thus reduced to one or two days.

By means of the hormonal test we can diagnose not only the normal but as well the pregnancy which pathologically has changed into hydatiform mole or its sequela, a chorionepithelioma. The hydatid degeneration of chorionic villi is associated with exaggerated production and elimina-

tion of prolan. Quantitative analysis of the prolan contents of the urine permits exact diagnosis.

The positive prolan findings in cases of chorionepithelioma led to further studies on tumors. These investigations showed that we were dealing with a quantitative hormone problem. In patients with tumors prolan elimination lies somewhere between the physiologic and the greatly increased levels of pregnancy. While in healthy women the normal output averages 5 mouse units to the liter, it rises in the pregnant to 1000 times this quantity, and in the presence of tumors the increase is only from 20 to 30 times that in the normal. These patients excrete approximately from 100 to 150 mouse units per liter of urine. To demonstrate these figures it is necessary to make use of the method of concentration (alcohol precipitation) which I have devised. It might be emphasized in this connection that the urine of carcinomatous patients will produce in the mouse practically only HVR I, very rarely II and III. This urine contains almost only follicle maturing hormone A. This phenomenon, however, is of no diagnostic value because the same reaction may be found in patients suffering from benign neoplasms. Nevertheless conditions are different in malignant newgrowths of the genitalia. While in benign genital tumors of women an increase of prolan A elimination is noticed in about 20 per cent of the cases, this incidence rises to 36 per cent in extragenital cancers and to 80 per cent in malignant genital neoplasms. Thus it is evident that the degree of hormone elimination is dependent not only upon the malignancy of the growth but also on its particular location. Naturally the question arose whether these hormonal changes are limited to genital carcinomas only in woman. Quantitative studies of prolan in the urine of men with carcinoma of the prostate yielded negative results. Studies made early in 1929 showed that the urine in a case of testicular carcinoma, contained both hormone A and B, exhibiting no difference therefore from that of a pregnant woman. Identical observations were reported by Fels and Matthias. Thus the fact is established that genital malignancy in man likewise creates special hormonal conditions. Omitting details I may state that the presence of the follicle maturation hormone (causing HVR I) in the urine of a man should arouse suspicion of a malignant testicular tumor. The reactions HVR II and III are of some value for the diagnosis of such malignancy, reactions which in women are characteristic for pregnancy. The factor which links these two phenomena to each other is that in most of the known cases, malignancy of the testicle was caused by a chorionepithelioma, though in rare instances also large celled seminomas of the testicle gave the same reaction. In two cases biologic proof of the presence of prolan in hydrocele fluid induced me to make a positive diagnosis of malignant neoplasm of the testicle, though the pathologist (Professor Anders) on the basis of histologic study was unable to make



this diagnosis, for cytologic examination of the puncture fluid did not show cells characteristic of malignancy. At least in these two cases the hormone-biologic test proved its superiority over the common cytologic search for typically malignant structures.

If implantation of very small particles of the suspected growth (0.05 to 0.1 gram) or injection of small amounts of tumor extract produces HVR II and III, then the diagnosis of malignancy can be made. This we succeeded in doing in instances of chorionepithelioma both in women and men.

These investigations have supplied the first foundations for a new procedure which I would designate as "Hormonal Tissue Diagnosis." Reactions initiated in an animal, consisting of follicular hemorrhages and luteinization, under certain conditions reveal the growth characteristics of implanted human tissue, that is, permit conclusions concerning its malignancy.

We may also mention briefly that prolan inhibits tumor growth (mouse carcinoma) so that in subsequent transplantations only little or no growth is noticed.

Finally I wish to call attention to a possible diagnostic value of increased elimination of follicle maturing hormones in the sexually mature woman. The hypophysis pours out these particular hormones at the time when function of the sexual gland ceases. Thus I found such increased elimination in the climacterium, the polyprolanic state. Operative removal of both ovaries in the mature woman is followed within two weeks by appearance of hormone A in the urine. If part of an ovary was intentionally preserved a hormonal test of the urine can later prove whether this rest is functioning or not. In examination of urines whose sources were unknown to me, I could isolate those from castrated women. I might mention that an increased prolan output was found in a young man three weeks after operative castration. It seems that this phenomenon in the human being represents a biologic law, making it possible to ascertain the activity or inactivity of the sex glands. In animals, conditions seemingly are different. While I could not find increased hormonal secretion in the urine of castrated mice and cattle, this was easily possible in the case of castrated rats and horses. How can this change in prolan production through castration be explained? (1) Prolan manifests its influences in the ovary. With removal of the ovary, prolan is deprived of its sphere of activity and thus uselessly produced it might leave the body by way of the secreted urine. (2) The sexual gland, as previously explained, can act as an inhibitor on the anterior lobe. With elimination of all such inhibition, one might assume, the anterior lobe will produce more hormones, which then find their way into the urine. This theory is supported by the discovery of Evans, confirmed by our observations, that the hypophysis of castrated animals actually contains more hormones. It is possible that both these

factors are actually at play after castration, that is to say, deprivation of the field for the activity of the follicle ripening hormones and removal of an inhibitor of hypophyseal hormone production by the sexual glands.

(For discussion, see page 932.)

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## SOME EXPERIENCES IN THE DIAGNOSIS AND TREATMENT OF CONGENITAL ANOMALIES OF THE FEMALE GENITAL TRACT\*

BARTON COOKE HIRST, M.D., PHILADELPHIA, PA.

IF ONE could make an important announcement hitherto unknown, based on original research, he might face an audience of his colleagues with more assurance than I feel at present. But such an opportunity rarely falls to any one's lot. Or if he had long been engaged in an investigation with which his name had become associated he might always be heard with interest and advantage. Unfortunately I belong to neither class so that the choice of a subject that might be worth your attention is difficult. The difficulty is increased by what seems to be a temporary pause in the surprising advance of recent years. Even the endocrinology of the menstrual cycle, the latest subject of intensive study appears to have approached a conclusion with Lepine's announcement of his separation of Prolan A from Prolan B, and with the practice now being adopted of providing oneself with the sex hormone for therapeutic use from the urine of one's own pregnant patients, thus dispensing with commercial products, and obtaining a more accurate dosage.

In doubt as to what to talk about, it occurred to me, in reviewing a long medical career, to ask myself in what class of cases there had been the greatest difficulty in diagnosis, the greatest difficulty in selecting off hand the appropriate treatment and the least help in medical literature for standardizing our conduct. Any student of gynecology, it seems to me, in propounding such a question to himself must find the answer in congenital anomalies of development in the female genital tract. They are all described in comprehensive treatises on gynecology, it is true, but little is to be found anywhere on the vagaries of their presentation in individual cases, nor of the treatment of bizarre examples not at all conforming to the usual types. Hence an excursion into medical casuistry may be forgiven in the study of these conditions, although the mere recital of cases is usually tedious and unprofitable. But after all, what is experience but the sum of individual cases.

An alternative subject appealing to me is the curious appearance of cancer in the pelvic and adjoining bones during the puerperium seen

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\*Read at a meeting of the Brooklyn Gynecological Society, April 1, 1932.

lately as a metastasis from an unsuspected primary growth, manifesting itself in a total inability to rise from bed or to walk, and regarded as hysteria. Another possibility was an analysis of hundreds of temperature charts, substantiating the claim in favor of the active treatment of septic abortions.

The selfish motive, however, of acquiring additional vicarious experience by listening to observations of congenital anomalies made by the members of the Society, dictated the choice of the subject of this communication.

As an example of the obscurity of some of these developmental anomalies in the female genital tract, how would one interpret the following symptoms, history, and physical findings?

A young nullipara seized with chills, fever, and abdominal pain was operated upon two and one-half years ago by a general surgeon for appendicitis. No acute appendicitis was found. A few weeks after returning from the hospital, coincident with a period, chills and fever returned and for the first time the urine was described by the patient as having a black color, with particles of solid matter in it. This phenomenon recurred with each period for the next six months, the discolored urine appearing usually a few days before or after the period, always with considerable fever, and at no other time in the month. She was returned to the gynecologic department of the general hospital in which she had been operated upon for a study, continued for six weeks, including repeated examinations: cystoscopy, pyelography, microscopic examination of catheterized and normally evacuated urine. The latter had a few blood cells and pus in it, the former contained none. The patient was finally discharged without a diagnosis.

Entering my service in the Graduate Hospital all these examinations were repeated without result, and the patient was about to be discharged as a malingerer when one day just before an expected period, in a final examination, a queer material was noticed on the glove of the examining hand: semisolid, dark brown in color, looking almost like dehydrated, decomposing blood. A closer investigation showed this material was oozing from the external urinary meatus and that its origin was from a distended pouch alongside the urethra. On opening the latter a considerable quantity of the dark colored material was expressed. Investigating the depth of the sac a uterine sound passed into a sinus some four inches or more upward and to the left. Suspecting a possible endometrial implant, the abdomen was opened and the pelvis searched for a possible endometriosis, but none was found. In a cursory examination of the pelvic organs themselves, they appeared to be normal. The sac in the neighborhood of the urethra and communicating with it was dissected out. The sinus extending upward and outward was curetted with a small, sharp curette. The patient reappeared seven months later reporting that there was no more fever with the periods, that the dark discoloration of the urine had ceased but that with each period a day or two before or afterward there was a discharge of bright blood independent of the period itself.

Reporting a year later all symptoms had disappeared and the patient had no discomfort. An examination showed a hollow space where the sac had been and the sinus had closed.

Speculating on the possible explanation of an unusual train of symptoms, which had interested me at the time but had been forgotten, it seemed possible that there had been a rudimentary development of the left müllerian duct as far at least as the uterine cavity and vagina were

concerned; possibly a condition analogous to a uterus bicornis rudimentarius solidus on one side, or perhaps a duplicity in the canalization of one müllerian duct, which has been noted. A uterograph was taken at this time, showing a typical picture of uterus unicornis.

Why there were no symptoms in this case until she had reached the age of twenty-five is inexplicable. Whether the appearance of the anomalous menstruation had anything to do with the appendectomy is difficult to say, but probably not. At any rate the treatment proved satisfactory, although adopted in haphazard fashion without adequate knowledge of the true condition. In fact the explanation just offered might be criticized as little more than a surmise. Nevertheless it is the only one I can think of. Here is another clinical puzzle.

A young nullipara, married a year, twenty-one years of age, was brought to the University Hospital with an acute abdominal condition thought by her physician in the country to be a ruptured ectopic pregnancy. She had begun to menstruate at the age of fifteen and the periods had been regular ever since; there was no missed period. She had been seized with severe abdominal pain at the time of an expected period. Her physician found an abdominal enlargement as great as that of a six months' pregnancy, very sensitive on pressure. The patient seemed shocked.

In my examination the vagina readily admitted two fingers: the cervix could not be reached. There was a tumor bulging the right lateral vaginal wall and vault, apparently continuous with the abdominal tumor reaching to the navel, firm in consistency and surrounded laterally and above by a corona of resonance. There were no symptoms of internal hemorrhage, no signs of pregnancy. But on account of the patient's acute suffering and some symptoms of shock an immediate section was done. There was difficulty in opening the peritoneal cavity as the anterior peritoneal reduplication was lifted to the level of the navel, but on entering the abdominal cavity an explanation of the unusual symptoms was found in a complete uterus didelphys perched on the top of an enormous hematocolpos in one atresic half of the double vagina in which the menstrual blood from one of the uterine bodies had accumulated for six years. There was no hematometra nor hematosalpinx. The other half of the vagina, perfectly patent, communicated with the left half of the double uterus. Hence the apparently normal menstruation.

An incision was made in the right vaginal wall below the peritoneal reduplication and a counter opening made just within the vulva. Both openings were drained with a large caliber stiffwalled rubber tube. The accumulated menstrual blood was thoroughly washed out. The upper tube was removed after a few days. The lower tube remained for some time to secure permanent patency of the atresic vagina which was found to be maintained a year later.

The father of the girl, a physician present in the operating room during the operation, asked what the prospects were should his daughter become pregnant. The two uterine halves were distinctly infantile in development, so I expressed the belief that pregnancy would terminate probably in an early miscarriage or possibly in rupture. At his urgent request therefore I sterilized her by double salpingectomy and the removal of the interstitial portion of the tube by exsecting both cornua. Curiously enough she reported a year later that she had never menstruated since, though both ovaries remained and very little if any endometrium was removed by the exsection of the cornua. Otherwise she had nothing to complain of.

One more case will serve the purpose of emphasizing the ever present possibility of these aberrant anomalies, confusing the diagnosis and making difficult the immediate choice of an appropriate treatment.

A young girl, aged thirteen, had begun to menstruate nine months before. The periods were normal. Four months after the establishment of menstruation she applied to the dispensary of physiotherapy for the diathermic treatment of specific endocervicitis. In the course of the treatment pain was complained of on the left side so she was referred to me to see if there was any tubal involvement. Finding a firm, spherical or fusiform mass at the site of the left tube, which however was not adherent, I believed the child had a small dermoid cyst and recommended operation. On opening the abdomen a perfect uterus bicornis was discovered with wide separation of the horns and the intervening uterine structure in the shape of a uterus incediformis. The tubes and ovaries on both sides were normal. During the child's previous treatment a slight tumefaction in the left vaginal wall and fornix was noticed but no attention was paid to it.

Two months later the child returned with increased pain on the left side and was then found to have an unmistakable cystic tumor occupying the left vaginal fornix, the upper part of the left vaginal wall and reaching three fingerbreadths above Poupart's ligament, apparently extending into the abdominal cavity. It was regarded naturally as an intraligamentary cyst. The abdomen was again opened but the cyst was below the pelvic diaphragm and could not be approached through the abdominal cavity. Besides it was in such close relation with the bladder that it appeared to be possibly a vesical sacculation. Distending the bladder with water the differentiation between the two was still more difficult. Again the abdomen was closed without doing anything. During the convalescence from the section the vaginal tumor was tapped with a long needle, its contents withdrawn by a piston syringe, proved to be pus with pure culture of *Staphylococcus albus*. Then both bladder and tumor cavity were filled with sodium iodide and an x-ray picture taken. It proved that an air distention of the bladder and sodium iodide distention of the cyst cavity would have made a better picture, but the differentiation between the two cavities was plainly established. A large opening was made into the cyst. Cyst wall and vaginal wall were sewed together and the cavity drained with a large caliber tube. The final follow up examination showed the inner cyst wall flush with the vaginal wall and clothed with vaginal epithelium.

Pretty certainly this was an unusually large cyst of Gärtner's duct extending higher into the base of the broad ligament than usual. As is well known, the persistence of the wolffian duct is twice as frequent in duplicity of the genital tract as in a perfectly fused and single genital tract. How it became infected is a mystery. Curiously enough at no time had the patient any rise of temperature whatever.

Without a tedious citation of other obscure cases of developmental anomalies to sustain the contention that we must be prepared to meet conditions under this head baffling the first attempt at diagnosis, in addition to many easily recognized off hand, allow me to present briefly another interesting phase of the subject, namely, What should be the ultimate collective judgment of the profession as to the propriety of some of the methods of treatment proposed, in regard to which there is at present difference of opinion.

Passing with a mere mention such obviously indicated procedures in one's practice as converting two uterine cavities into one by splitting the septum of a septate uterus, treating similarly a double vagina, uniting the cervix of a uterus unicornis with a huge hematometra to an artificially constructed vagina and so on, it would interest me greatly

to hear the views of the members present on certain moot questions in the treatment of absent vagina and uterus. I confess to a prejudice against using a segment of intestine or rectum by an operation attended with some risk, merely to permit coitus: but it must be owned that the other proposals to establish an artificial canal for that purpose have been usually unsatisfactory. I have tried most of them, I think, including implanting the vagina from one woman into another. In the last mentioned case the woman with the implanted vagina left the hospital in two weeks with a canal lined with mucous membrane, admitting the full length of a bivalve speculum of considerable size. But a sufficiently long continued follow up observation of these cases usually shows, I think, shrinkage both in length and breadth of the artificial canal. What I had particularly in mind to ask is, in those cases of absent vagina and uterus encountered occasionally, in which coitus is practiced by the urethra, after prolonged and gradual dilatation, without apparent harm to the woman, should she be allowed to continue that practice? I recall a case in which a two-finger examination through the urethra was easily practicable. The married couple, having lived together some years, were unaware of any anatomic peculiarity. Their sexual relations were said to be satisfactory. The woman came to me for sterility. She was a poor surgical risk and did so badly in an attempt to utilize a segment of the rectum for an artificial vagina that the operation was given up. She refused further surgical intervention. Meanwhile a cystoscopy showed no disease of the bladder and there was no incontinence of urine. The patient disappeared and I have no means of learning her subsequent history. I have often wondered if in such cases injury and infection of the bladder could be indefinitely avoided and, if that were so, whether we would be justified in letting well enough alone.

One must be prepared for some ethical questions in these cases of absent vagina and uterus that are not so easily answered.

A young girl, perfectly formed in other respects, but with no uterus or vagina, and about to be engaged to an eligible young man, was brought by her mother who asked first whether it was possible to correct the congenital defect, and secondly, whether the prospective fiancé should be informed of the girl's condition. To the first question a negative reply would be given by most of us, I think, in the case of a young woman for whom married life would not begin for a number of months. The second question was hardly fair to put to a physician for a medical opinion, but as a matter of ethics alone there could, it would seem, be only one answer. A colleague however differed from me and the girl was operated upon. As a social as well as a medical problem it would have been interesting to learn the result, but I had no means of doing so.

In contrast with this controversial subject of absence of the lower genital tract it is a relief to turn to another congenital defect in the female, anus vestibularis incorrectly so-called, for as we all know the anus in these cases is in the fossa navicularis. Very few physicians can

have much experience in handling this defect for it is rare. The combined statistics of Von Bardeleben and Stoeckel show only one for each in 63,000 births. Fortunately the diagnosis is unmistakable and the treatment is easy, safe and the result usually satisfactory. I happen to have operated upon a young child and a young girl with this condition. By a fairly deep median perineal incision, a circular incision around the anus to mobilize it, with care to make the lateral incision somewhat superficial to avoid the anal nerves so as to preserve continence, the anus is pushed back to its normal position and the perineal incision closed in front of it.

Even the most superficial review of congenital defects, such as this necessarily is, would be incomplete without some reference to their effect on childbirth. There is not so much to be said on this part of the subject for many of these defects preclude conception, and professional opinion is pretty well in accord as to their management in parturition. For a most excellent statistical, clinical, and historic study of duplicity of the genital tract in pregnancy and childbirth one could not do better than to consult the analysis of 35 cases among 141,946 childbearing women in the report of the Lying-In Hospital of New York of March, 1932. With one of the conclusions in this paper I am in hearty agreement. "The necessity for operative correction has been greatly exaggerated."

Some years ago two cases of cesarean section for labor in a double uterus were reported, at a meeting of the American Gynecological Society, and I regret to remember that in the discussion I added two more for I am not at all sure they were necessary. It is the bulk of the nonpregnant uterus that is usually regarded as an insuperable obstacle demanding section, but we have all seen natural labors in these cases. There is little difficulty in the diagnosis except perhaps by the inexperienced. I recall an amusing consultation in which a general practitioner was doubtful of his sanity, for on one examination he found a rapidly progressing labor and on another all signs of progress had disappeared.

It must not be assumed, however, that all these cases may be regarded with indifference. The incidence of legitimate indications for operation is high, as is that of numerous complications and in some cases unexpected difficulties are encountered in conditions that appear easily manageable. As an example I recall a transverse fetal position in a uterus incurvatus, the interior of which more closely resembled a uterus bicornis, which is often the case. A version appeared perfectly practicable but the head was so impacted in one horn and the shoulder in the other that the fetus could not be budged and a cesarean section was necessary with the added danger of a precedent intrauterine manipulation.

# AVERTIN ANALGESIA IN OBSTETRICS

## A REPORT OF ONE HUNDRED AND FIFTY CASES\*

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IN ORDER to evaluate the effectiveness of "avertin" or tribromethyl alcohol as an analgesic agent during labor, a study of one hundred and fifty cases was made on the obstetric service of The Brooklyn Hospital. The anesthetic properties of this drug were demonstrated by Eichholtz<sup>1</sup> in 1927. During the past four years, it has been widely used, especially in Germany, as a basal anesthetic for surgical operations, and numerous clinical and experimental studies concerning it have appeared. Very little work comparatively, has been done in its use as an analgesic agent for the parturient woman.

H. J. Stander,<sup>2</sup> following his studies on avertin in dosage amounting to 100 mg. of drug per kilogram of body weight, found no changes in blood chemistry in the nonprotein nitrogen, urea nitrogen, uric acid, lactic acid, creatinin, chlorides, or carbon dioxide combining power, and only a very slight increase in blood sugar. However, in view of the manner in which avertin is detoxicated in the liver,<sup>3</sup> it does not seem advisable to use it in such conditions as eclampsia, in which liver injury is an outstanding factor.

Stander, however, observed no evidence of liver necrosis in dogs, when a dose of 500 mg. per kilogram was used. Bearing this in mind, it was decided in the study of avertin to use the drug in no patient giving evidence of toxemia.

*Dosage.*—The dangers have been fully enumerated by a number of German surgeons<sup>4</sup> who pioneered in its use, and there can be no doubt that their mortality rate has been due to overdosage, which in turn has been due to the effort to induce anesthesia with avertin unsupported. This is neither necessary nor advisable. Once given avertin is rapidly absorbed, and beyond control. To obtain the best results with safety, an average dose should be given, and any remaining deficit in the anesthesia of the second stage of labor should be made up by nitrous oxide and oxygen inhalation. Also, in some cases of cesarean section when an inhalation anesthetic is to be avoided, local anesthesia may be the supplement of choice. Other factors also enter the problem of dosage for the parturient woman, such as the effect of the drug on the baby, the uterine contraction, length of labor, and so on.

Our first attempts were made with one-half the surgical dose, or 50 mg. per kilogram. This was later increased to 60, then 80. In one of our three cesarean cases 100 mg. per kilogram was used.

\*Read at a meeting of the Brooklyn Gynecological Society, April 1, 1932.



*Administration.*—No attempt was made to select the patients. As soon as labor was definitely established with regular pains, and beginning dilatation of the cervix, two procedures were tried; one with a preliminary hypodermic injection of morphine and scopolamine, the other without these. The result in general seemed better with the first plan, so that the routine finally adopted is: Morphine gr. 1/8, scopolamine gr. 1/200, hypodermically, which is repeated at about two-hour intervals until the cervix is effaced, and dilatation has progressed to about one inch. At this time a 60 mg. per kilogram dose of avertin is administered into the rectum, with the caution of introducing the catheter above the presenting part if it happens to be in the cavity of the pelvis, and starting the injection immediately after the cessation of a uterine contraction. This precaution usually insures against expulsion of the drug, as the absorption of the drug is very rapid, and even though the water vehicle may be subsequently expelled, the desired effect of the drug is obtained.

The state of amnesia is usually maintained from two to four hours, while the analgesia is prolonged to six or eight hours in varying degree. After three hours the dose is repeated without hesitation. The intention is to give the second dose just before the beginning of the second stage. In two cases of long labor a third dose was used.

Successful amnesia and analgesia is obtained with any agent only by constant and thoughtful observation of the progress of labor. No two cases are exactly alike, but with the skill acquired by the observation of many cases, complete amnesia and analgesia can be obtained in the majority of cases. When failures occurred, it was the result of inaccurate observation of the progress of labor, or timidity as to the use of sufficient amount of the drug.

*Action.*—An excellent result was obtained with 60 mg. dose. With the 80 mg. amount there was noted diminution in the strength of the contractions of the uterus, a longer interval between pains, and a consequent prolongation of the labor. With the smaller dose of 50 mg., insufficient analgesia and amnesia were obtained. On the average, the action of the drug was manifested in fifteen minutes. The patients became drowsy, slept through pains, and were oblivious to their surroundings. Many of them do not remember being transported from the labor room to the delivery room. The general condition of the women was excellent. No cyanosis was noted. There was no noticeable change in pulse or respiration. Dandy<sup>5</sup> and White<sup>6</sup> using 100 mg. per kilogram, reported a distinct fall in blood pressure. In this series of cases using a smaller dose, no appreciable drop was recorded. A few of the cases were quite irrational. The resultant restlessness often required additional nursing. The fluid intake and output was normal. There was no evidence of rectal irritation.

*Labor.*—In this series, five-sixths of the patients were primiparae,

but no prolongation of labor was noted. The average duration was: primiparae: first stage, fourteen hours, (the longest, fifty-eight hours, shortest, four hours). Second stage, one hour and ten minutes. Multiparae: first stage, seven hours. Second stage, twenty minutes. Brown<sup>8</sup> reporting on the use of pernocton in one hundred and thirty cases, records the average length of labor as eighteen hours.

Hamblin and Hamblin<sup>9</sup> in their paper on "The Oral Administration of Sodium Amytal," in 50 cases noticed no prolongation of labor, as their average length of labor for primiparae was fourteen hours. Schoeneek<sup>10</sup> using Gwathmey ether in oil routine, in two hundred and forty-five cases at The Brooklyn Hospital, found the average first stage of labor to be fourteen hours. It would seem that avertin compares favorably with these other agents, in that labor is not prolonged, and the efficiency of the uterine contraction is not decreased. However, it was noticed that shortly after the administration of the drug, the interval between pains was lengthened for a short time.

*Delivery.*—The presenting part was noted in 117 cases as a vertex with the occiput anterior; in 26 cases as occiput posterior, and in 7 cases as a breech.

The method of delivery was, cesarean section 3; high forceps 1; low forceps 12; forceps control and perineotomy 101; spontaneous vertex 26; spontaneous breech 3; breech extraction 4. With the high incidence of forceps control it is rather hard to judge the duration of the second stage. We are of the impression that in a number of cases there was a definite retardation of the progress of labor in the second stage. The contributing factors were a diminution in the strength of contractions, increased interval between expulsive pains, and the depth of analgesia, with its loss of cooperation.

Many individuals obeyed instructions to bear down, yet on questioning the next day failed to remember their experience in the delivery room. In general the patients were quiet and easily managed.

The amount of anesthetic was greatly reduced. Except in a few incidences a supplemental inhalation of nitrous oxide and oxygen was given at the time of actual delivery and for perineal repair. In 10 cases delivery was accomplished without the use of inhalation anesthesia.

Avertin is a great aid as a basal anesthetic in the performance of cesarean section operation. We used the 80 mg. dose, supplemented by nitrous oxide and oxygen in two cases, and local anesthesia in the third case.

*Babies.*—Six of the babies required resuscitation. The others showed no evidence of cyanosis or narcosis, each breathing and crying vigorously immediately after birth. There were 4 stillbirths.

Analyzing the stillbirths, only one could possibly be attributed to avertin. The first case was a breech presentation; the patient was admitted to the hospital with a prolapsed pulseless cord. The second was a syphilitic patient, and on admission

no fetal heart was heard. The third was a primipara who had a fifty-eight-hour labor and was brought to the hospital after being in labor forty-five hours at home. Examination revealed a complicating undilated cervix, bronchopneumonia, foul amniotic fluid, and a persistent occipitoposterior position. Her condition on admission was recorded as serious. After complete rest with morphine and bromide and chloral per rectum, labor advanced to full dilatation of the cervix. About twenty minutes before delivery a 100 mg. dose of avertin was given, and supplemented by a small amount of nitrous oxide and oxygen. The fetus was delivered with axis-traction forceps, and the patient later recovered and was discharged from the hospital. We feel that this case was a real indication for the use of avertin.

The fourth stillbirth was a premature infant weighing five pounds. Avertin was given one hour before delivery. The patient experienced a very rapid second stage, with exceedingly hard contractions. The delivery was spontaneous. Immediately following its birth, the baby took several gasps, but all means of resuscitation failed. Autopsy was refused. We are in doubt as to whether this was an avertin death or the result of prematurity, cerebral hemorrhage, or atelectasis.

*Results.*—The results of our experiences with these 150 cases were tabulated after the method of the Boston Lying-In Hospital.

Of the 32 cases receiving two doses of avertin: 5 remember clearly; 15 remember vaguely, and 17 remember nothing concerning their labor. Two cases receiving 3 doses remember vaguely. One hundred and fifteen cases received one dose: 20 of these remember clearly, 65 remember nothing, and 30 vaguely remember their experiences.

Of the 25 who remember clearly, 20 said they had a hard or moderately hard time. The other 5 said they had an easy time, and that they had received considerable relief from the medication.

#### CONCLUSIONS

1. Avertin is apparently a safe analgesic agent.
2. The best results were obtained with a 60 mg. per kilogram dose.
3. Its use does not prolong labor or increase the incidence of operative delivery.
4. Avertin produces a successful state of analgesia or amnesia in the majority of cases.

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# FETAL MORTALITY AND BREECH PRESENTATION

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NO STUDY which inquires into the results of a condition leading to a 10 per cent to 15 per cent fetal mortality requires justification. Bad results in cases of breech presentation are too apt to be ascribed to a more or less unavoidable condition and, as such, viewed complacently. That such complacency is not due to negligence but rather to the fact that the defects in our management of cases of breech presentation are not glaring and are therefore difficult to combat, is apparent. Impressed by the high fetal mortality in breech presentation, I have made a critical study of the 301 breech deliveries that occurred in 8509 deliveries in the University of California Hospital. I feel that this study has brought out a number of facts which should aid us to improve materially our treatment and that they are, therefore, worth recording.

*Incidence.*—The 301 breech presentations constitute 3.53 per cent of the 8509 deliveries, a percentage that corresponds closely with those reported in other series. Since 16 of these breech presentations occurred in women delivered by cesarean section and presented no problem of delivery, they are not included in the calculations for fetal mortality, etc. The exclusion of the 16 cases leaves 285 for consideration, of which 125 occurred in multiparae and 160 in primiparae. Authorities are generally agreed that breech presentation is more common in the multipara than in the primipara but, curiously enough, the incidence in this series was 3.9 per cent for primiparae and only 2.8 per cent for multiparae.

*Viability.*—Not all babies delivered by breech were viable, and there were some babies which were dead on admission to the hospital. By viable, we mean arbitrarily all babies weighing 1500 gm. or more which were living when the patient was admitted to the hospital, in the absence of marked abnormalities incompatible with life, such as spina bifida, hydrocephalus, etc. Of the 285, 256 were viable, 29 dead or non-viable, as shown in Table I.

TABLE I. FETAL VIABILITY

	TOTAL CASES	DEAD OR NONVIABLE FETUS	VIABLE FETUS
Primipara	160	12	148
Multipara	125	17	108
Total	285	29	256

*Weight of Babies and Duration of Labor.*—The average weight of 228 viable babies was 3144.4 gm., 300 gm. less than the average for the clinic. The largest baby weighed 5075 gm. The average length of labor was 10.59 hours for multiparae, and 16.41 hours for primiparae, both slightly less than the averages commonly stated in textbooks.

*Fetal Position.*—The exact positions and their frequencies are tabulated in Table II, on the basis of the total 301 cases. They require no comment.

TABLE II. POSITION

POSITION	TIMES	PER CENT
L.S.A.	134	44.5
R.S.A.	89	29.5
R.S.P.	39	12.5
L.S.P.	26	8.6
Undifferentiated	13	4.9
Total	301	100.

In 278 cases mention was made whether the child presented as frank breech, etc. Frank breech occurred 187 times or 67.3 per cent; footling breech occurred 75 times or 26.9 per cent; complete breech occurred 16 times or 5.8 per cent.

*Diagnosis and Conversion.*—In 118 of the 285, or almost one-half of the cases, a diagnosis of vertex presentation was made at the last outpatient clinic visit before delivery. Whether these figures represent a true state of affairs or not is difficult to say: often the patients did not return when requested, and this last clinic visit occasionally was even one month prior to delivery: moreover, fourth year students occasionally made the last abdominal examination on patients who had been coming regularly to the clinic and who had previously been found to be normal. In an additional 63 cases, no diagnosis was made, usually because the patient was not seen until late in labor. In 104 cases a diagnosis of breech presentation was made prenatally, and an attempt was made to convert 20 of these to vertex. The attempt proved futile in 16, and in the remaining four the breech presentation recurred. Unfortunately, a perusal of the prenatal records of the entire 8509 cases would be necessary to determine the number of cases in which conversion to vertex presentation was successful and permanent. That conversion of a breech to a vertex presentation is worth while is undeniable, since fetal mortality in vertex presentation is so much less than in breech, and the chance of harming the fetus in performing the maneuver is exceedingly slight. However, in a large proportion of cases, the diagnosis of breech presentation is so confusing or the presentation occurs so late in pregnancy that the question of conversion either does not arise at all, or the maneuver becomes actually impossible by the time the diagnosis is made. These facts make of it a method of treatment which we may or may not be able to use, but one on which we can never depend.

*Fetal Mortality.*—Of the 256 viable babies, 24 were stillborn, and 14 died in the hospital between ten and fourteen days after delivery, making the total mortality 38, or 14.8 per cent. Of the 38 dead babies, 20 were fullterm (weighing over 2500 gm.), and 18 were premature (1500 to 2500 gm.). The distribution between multiparae and primiparae, term and premature, etc., is shown in Table III.

TABLE III. FETAL MORTALITY

VIABLE	STILLBORN		DYING IN HOSPITAL		TOTAL	PER CENT
	TERM.	PREM.	TERM.	PREM.		
Multipara 108 cases	6	3	0	7	16	14.8
Primipara 148 cases	12	3	2	5	22	14.8
256 cases	18	6	2	12	38	14.8

Two facts stand out clearly: (1) that breech delivery was rarely, if ever, responsible for stillbirth in the premature cases, and (2) that fetal stillbirth at term was almost invariably associated with birth trauma. This is shown by the following. Of the 18 premature fetal deaths, 12 occurred *after* birth, mostly with such diagnoses as prematurity, aspirative pneumonia, respiratory failure. Of the 6 stillborn, in no case was there difficulty with the delivery sufficient to explain the death. Moreover, three occurred in multiparae and 3 in primiparae. On the other hand, of the 20 fetal deaths at term, 18 were stillborn, and only two occurred later, one of these from an intracranial hemorrhage. In short, 19 of the 20 fetal deaths at term were definitely associated with birth trauma. Further testimony to this fact is that 14 of the 20 fetal deaths at term occurred in primiparae, in which one would expect to have more difficulty with the delivery.

Following this line of thought, if we separate the pregnancies at full-term from those premature, we get the amazing figures shown in Table IV.

TABLE IV. FETAL MORTALITY AT TERM

VIABLE		STILLBORN	MORTALITY
At term	219 cases	20	9.10%
Premature	37 cases	18	48.6 %
Total	256 cases	38	14.8 %

From this table it would appear that a breech position carries an extraordinarily bad prognosis for a premature child. However, an analysis of the cases discloses no reason for the high mortality since there was no difficulty encountered in delivering any of the premature infants in a breech position. On the other hand, I found upon reviewing the premature fetal mortality for several years for all presentations, in-

cluding those dying in the hospital as well as those stillborn, that 88 died of the 239 premature babies, or 36.8 per cent. The difference between the figures 36.8 per cent and 48.6 per cent is 12 per cent which I feel represents the additional risk for prematures delivered by breech. It is gratifying, moreover, to find after excluding the premature cases that the fetal mortality in viable fullterm cases is but 9.1 per cent. Realizing that the prognosis for prematures is bad at best, and having learned that the majority of the premature deaths occur after delivery and apparently unassociated with it, we naturally feel less responsibility for them than for those occurring at term. The histories give no clue as to why these women fell into labor prematurely.

Analysis of the fetal deaths with respect to position revealed no significant association. The various positions were present in the fetal death group in about the same proportion as those cited for the entire series. In this group, frank breech occurred in 63.8 per cent, footling breech in 33.3 per cent, and complete breech in 2.9 per cent, figures which also tally closely with those for the complete series. Likewise, the divisions into term and premature, actual stillbirths and neonatal deaths, retained proportions closely parallel to those stated for the total number of cases. Apparently fetal mortality in breech presentation is uninfluenced by position.

*Mode of Delivery.*—In an effort to ascertain the reasons for fetal mortality, the various modes of delivery are tabulated, together with their accompanying mortalities, in Table V.

TABLE V. MODE OF DELIVERY

TYPE OF DELIVERY	TIMES	FETUS ALIVE	STILLBORN			FETAL MORTALITY PER CENT
			TERM	PREMATURE	TOTAL	
1. Spontaneous	15	8	1	6	7	46.6
2. Breech extraction Mauriceau	219	191	16	12	28	12.7
3. Forceps on aftercom- ing head	20	17	3	0	3	15.0
4. Forceps on breech	2	2	0	0	0	00.
Total*	256	218	20	18	38	14.8

\*Omitting dead and nonviable fetuses.

The following points deserve comment: (1) regarding the actual mode of delivery: other methods than breech extraction followed by the Mauriceau maneuver, the usual mode in this clinic, were not employed sufficiently often to justify comparison with it; (2) in the spontaneous cases over which we have little if any control, there was a high fetal mortality for which the obstetrician was not actually responsible. Three of

the stillborn prematures in this group were not actually stillborn but died later in the hospital. The one fullterm stillborn was due to an accident: the woman called the hospital too late in labor for the physician to arrive in time for the delivery. Upon arrival, he found the baby born, except for the head which had remained in the vagina for some fifteen minutes, without either the patient or her husband making an effort to extract it; (3) in Group 2, eight of the 28 total stillborn or almost one third, occurred in cases in which labor had been induced (six by bag). Eight, or two-thirds, of the 12 stillborn prematures were babies which died in the hospital after delivery; (4) in Group 3, two of the three fetal deaths occurred before we used the Piper forceps, and the operation was attempted rather as a last resort after ordinary methods of extraction had proved exceedingly difficult; (5) in Group 4, the operation was done once accidentally, the presentation having been mistaken for a vertex, and once purposely, in place of a fillet.

If we rearrange the table to exclude the prematures, we gain a clearer idea of the mortality for which the obstetrician may have been responsible and upon which we should be able to improve.

From a perusal of this table the inference is that, barring accidents and interference, the fetal results were relatively good; moreover, that bad results were not distinctly related to the actual method of delivery but were definitely related to efforts to induce and complete labor.

TABLE VI. MODE OF DELIVERY (EXCLUDING PREMATURES)

DELIVERY	VIALE- TERM	STILL- BORN	MORTALITY PER CENT	COMMENT AS TO FETAL DEATH
Spontaneous	8	1	12.5	An accident
Breech extraction	192	16	8.3	Six after induced labor (five by bag). Manual dilatation completing the cervical dilatation in 4 of the 5 cases
Forceps on aftercoming head	18	3	16.6	Two of the three as last resort with ordinary forceps
Forceps on breech	1	0	0.0	On purpose in frank breech in place of fillet
Total	219	20	9.1	

## ANALYSIS OF DIFFICULTIES

Induction of labor, completing the dilatation of the cervix manually, and breaking up the breech at full cervical dilatation were three activities which appear to have been followed by disastrous consequences. Let us first indict and then excuse them for, of course, they had their indications and were tried usually in the cases which presented real obstetric problems.

*Induction of Labor.*—Labor was induced in 25 women of the 285, 21 of



which were carrying viable babies. Of the 21, seven babies, or one-third were stillborn (five at term, two premature). Table VII shows that sound justification is needed for a procedure which results in a 33.3 per cent fetal mortality. Obviously, the bag is largely responsible for this excessively high mortality.

TABLE VII. INDUCTION OF LABOR

METHOD	TIMES	ALIVE		STILLBORN		NON-VIABLE	MORTALITY PER CENT
		TERM	PREMATURE	TERM	PREMATURE		
1. Castor oil and quinine	9	8	0	1	0	0	11.1
2. Hydrostatic bag	11	0	1	4	2	4	85.7
3. Castor oil and quinine, rupture membranes, nasal pituitrin	5	4	1	0	0	0	0.0
Total	25	12	2	5	2	4	33.3

The indications for inducing labor in those women are tabulated in Table VIII.

TABLE VIII. INDICATIONS FOR INDUCTION OF LABOR

INDICATION	TIMES	ALIVE		STILLBORN		NON-VIABLE
		TERM	PREMATURE	TERM	PREMATURE	
1. Toxemia	5	1	0	0	1	3
2. Past term	4	3	0	1	0	0
3. Premature rupture of membranes	5	3	1	0	0	1
4. Pelvic contraction	1	0	0	0	1	0
5. Questionable or unknown indication	5	1	0	4	0	0
6. Experimental method of induction	5	4	1	0	0	0
Total	25	12	2	5	2	4

17 viable term babies, 5 stillborn (4 after bag, 1 after castor oil and quinine)  
4 viable premature, 2 stillborn (both after bag)

In Groups 1 and 2, the indications are perfectly justifiable with two stillborn babies out of six viable. The average weight of the past term babies was 4120 gm. Groups 3 and 4 are open to question as justifiable indications, with one stillborn baby out of five viable. Group 5 should not have been induced; the indications for three of the cases were, (a)

two days overterm (baby weighed 8.2 pounds), (b) eight days past term (no weight, baby measured 48 cm. long), (c) "slight toxemia, two weeks premature" (the toxemia consisted of a mild elevation in blood pressure without other signs or symptoms). In the two remaining cases, no indications could be found. In this group there were five viable babies of which four were born dead.

*Manual Dilatation of the Cervix.*—In six cases, some degree of manual dilatation of the cervix was carried out (usually to complete dilatation of the cervix, already 6, 7, or 8 cm. dilated). Four, or two-thirds of the babies were stillborn. All these women were at term. Four of the six labors were induced, twice by castor oil and quinine, and twice by hydrostatic bag, a further indictment of the induction of labor. Three of the induced labors resulted in stillborn babies. The reasons for the manual dilatations are tabulated in Table IX.

TABLE IX. REASONS FOR COMPLETING THE DILATATION OF THE CERVIX MANUALLY

REASON	TIMES	RESULT
Poor pains	3	One stillborn (1 after bag, 1 after castor oil and quinine, 1 spontaneous)
Fetal distress	2	Two stillborn (1 after castor oil and quinine, 1 spontaneous)
Maternal distress	1	One stillborn (after bag)
Times	6	Stillborn 4

The average length of labor in this group was 31.13 hours, the longest being 48 hours, showing, as justification for manual dilatation, that these cases presented a problem, any solution of which might have been incorrect.

*Breaking Up the Breech at Full Dilatation.*—Although this procedure is recommended as a routine by some, the contention being that it gives the obstetrician a leg to pull on if it becomes necessary to extract the child in a hurry, I feel that it is an unusually bad thing to do. This procedure was deemed necessary five times and three of the babies were delivered stillborn. The reasons are presented in Table X.

TABLE X. BREECH BROKEN UP AT FULL DILATATION

REASON	TIMES	RESULTS
Poor pains	3	Two stillborn (1 after bag)
Contracted pelvis	1	One stillborn
No reason given	1	Alive
Times	5	Stillborn 3

The average length of labor was 22.1 hours.

If we place in one group those requiring manual dilatation and those in whom the breech was broken up at full dilatation, as women apparently in need of extraordinary procedures for successful completion of their labors, the seriousness of these procedures and the appalling fetal mortality they carry with them is brought home to us by the fact that in the 11 times these maneuvers were tried, there were 7 stillborns.

It is an important commentary, I think, that either one or the other of these procedures was considered necessary 6 times out of the total 11, because of poor pains. The significance of this statement will be discussed later. In this group of 11, labor was induced 5 times (3 by bag, 2 with castor oil and quinine), and 3 of these 5 were characterized by poor pains.

These figures show clearly that all three of these procedures lead to an unduly high percentage of bad results, so bad in fact that almost anything would be better. In justification for initiating the procedures, we have our indications, which cannot in all instances be vindicated, I think. Remedy for this sort of thing lies in much stricter indications for their employment and in abandoning the bag as a means of inducing labor except in cases in which the life of the child is not of great consideration.

*Other Difficulties in Delivery.*—It will be noted that attention has been directed particularly to difficulties arising in the earlier stages of labor rather than to the actual delivery. Most of what is written about breech presentation today concerns the actual delivery, but from a study of these cases, it would seem that it is the course and conduct of the pregnancy and earlier stages of labor which is all important, provided a reasonable technic is employed at delivery. It is true that, in delivering a large baby presenting by the breech, or a normal sized one through a moderately contracted pelvis, skill and a proper technic may determine whether the outcome be a happy one or otherwise; on the other hand, the management of the pregnancy and early labor determines whether a difficult situation shall arise or not. In other words, we should not allow our conduct of a case to precipitate a bad situation from which only extraordinary skill and luck can extract us.

*Forceps in Delivery.*—Difficulty in extracting the head was mentioned only twice as being the probable explanation of fetal death. It may be that this difficulty will not be encountered when the Piper forceps (or any other type of forceps on the aftercoming head) are employed routinely, but I doubt it. When serious trouble in extraction is met, it is usually because of the unduly large size of the head, or because the head is partially extended high in the birth canal, in neither of which contingencies is the Piper forceps of much use. Forceps are easily applied to the aftercoming head when it is low in the birth canal, and perhaps their application adds finesse to the delivery of the head; the Mauriceau maneuver, carefully performed, is perfectly satisfactory however.

Extension of the arms was mentioned once only as being a contributing cause of fetal death. This would not seem, then, to be a major difficulty. Though sometimes unavoidable, this accident is often due to an error in technic which should be avoided.

Excessive pressure on the head through the abdomen was mentioned once. Though moderate pressure from above is usually necessary to accomplish delivery of the head without excessive pulling from below, it should be applied carefully.

A contracted pelvis appears responsible for difficulty in delivery leading to fetal death in at least two cases. However, we have the following data concerning contracted pelvis. Contracted pelvises occurred 15 times in the 285 cases; in one the child was nonviable, and in four cases, stillborn babies were delivered (two at term and two premature). In the two term cases, the generally contracted pelvis was probably a decided factor in causing the fetal deaths (delivery of the aftercoming head by forceps was unsuccessfully attempted), although the cervix may have been a factor. Delivery in the two premature cases was easy and apparently unaffected by the contracted pelvis. The number and variety of pelvic contractions is tabulated below:

Generally contracted typical	8
Simple flat	3
Flat rachitic	2
Generally contracted rachitic	1
Funnel typical	1
	<hr/> 15

This review suggests the lack of wisdom in attempting to deliver a breech in the presence of any but the most minor pelvic contraction except by cesarean section.

Premature rupture of the membranes was known to have occurred ten times (not counting the five times this was done artificially as means of induction). In this group, there were two stillborn babies, both premature. Both died a few days after delivery. In one, there was placentitis, even though the membranes had ruptured only a few hours before the onset of labor; in the other, there was an infected cord, atelectasis, and a small tentorial tear (this labor had been induced by bag). Twice the membranes were ruptured artificially during the course of labor before full dilatation, and stillborn babies were delivered in both instances; the cord prolapsed in one of them. There is no better invitation for the cord to prolapse than to rupture the membranes after labor in breech is well started and before full cervical dilatation.

Prolapse of the cord occurred six times and with two of the babies stillborn. One of the fetal deaths occurred when the cord prolapsed following artificial rupture of the membranes before full cervical dilatation. The other happened in a case in which a bag had been inserted into the vagina inadvisedly.

Recently the policy of inserting a large sized Voorhees bag into the vagina in primiparae has been adopted, with the double purpose of preventing the membranes from rupturing early in labor and of dilating the birth canal, thus making the ensuing breech extraction easy. This procedure was employed six times, once inadvisedly (membranes already ruptured, footling presentation). It worked very well except in this one case in which the cord prolapsed, with resulting stillborn baby. The average length of labor was 18.75 hours.

*Birth Injuries.*—Others than those found at autopsy as the cause of fetal death, birth injuries were noted six times as follows:

Fractured humerus	2
Fractured femur	1
Fractured clavicle	1
Abrasion in groin	1
Hematoma of thigh	1
	<hr/> 6

None of these injuries occurred in large babies. This seems to be a very small percentage of injuries.

*Maternal Mortality and Morbidity.*—One woman died from postpartum hemorrhage after a live baby had been delivered by an easy breech extraction. The delivery took place at home several years ago: her condition became bad very rapidly in spite of the usual measures to control hemorrhage, and she died before she could be transported to the hospital. She had had four previous breech deliveries. One patient in the cesarean section group died of disseminated tuberculosis. Her early death was expected, the section being done in order to obtain a live baby from a woman almost at term, hopelessly and acutely ill with tuberculosis, and was in no way attributable to the operation. These two were the only maternal deaths.

Because of varying standards of morbidity, figures are given for the one employed in this clinic (a rise in temperature to 38° C. on one occasion in the puerperium), and also for the standard often employed elsewhere. There were no serious infections in the entire group, and, indeed, the great majority were only technically morbid.

TABLE XI. MORBIDITY

	NUMBER OF CASES	PERCENTAGE OF MORBIDITY
Temperature to 38° twice	43	15.43
Temperature to 38° once	66	23.15

## SUMMARY AND CONCLUSIONS

In this series of 285 breech deliveries, the fetal mortality in viable cases was 14.8 per cent, and was evenly divided between multiparae and

primiparae. When the mortality in premature infants, 48.6 per cent, was deducted, the mortality at full term was found to be 9.1 per cent, a figure for which the obstetrician may have been responsible, since there were no technical difficulties in delivering the premature children. The majority of fetal deaths occurred in cases in which there was some type of interference in labor, such as induction of labor, completing the dilatation of the cervix manually or breaking up the breech at full dilatation by traction, and not because of actual difficulty in delivery. An analysis of the various methods of delivery employed, while inconclusive because of the comparatively small number of variations from the usual method of breech extraction followed by the Mauriceau maneuver, did not show one method to be appreciably more advantageous than another. On the other hand, it was the course of the earlier stages of labor which determined the outcome of the delivery; either it was felt that labor must be induced, or there were poor pains and the dilatation of the cervix was manually completed, or for some other reason, a foot was brought down and the breech wedge was broken up when the cervix was in full dilatation; these were the cases which resulted badly. Because of these facts, I feel our conduct of the earlier stages of labor is all important, provided one employs a reasonably good technic at actual delivery. It is granted that labor complicated by poor pains often offers a problem, any solution of which might prove wrong; still, the facts just reviewed are the real problem, and as is shown in this study, indications for interference must be unimpeachable, since such procedures carry a very high fetal mortality. The outcome of our cases should become largely predictable from the characters of the early stages of labor. Indications for cesarean section should be carefully reviewed if there is reason to believe that the labor cannot be terminated without the aid of various means of interference from below.

Maternal mortality was negligible; maternal morbidity, though technically high, was due almost entirely to trivial infection.

One further plea; that the bag be abandoned as a means of inducing or hastening labor, except in cases in which the life of the child is of no consequence.

There are a sufficient number of bad results in this series of cases to demand explanation, and indeed a lesson is forthcoming. On the other hand, the situation is not a gloomy one when it is considered that these cases were not uniformly delivered by residents but more often were handled by a succession of young house officers in training.

The total mortality for recent years, in which two-thirds of the viable cases were delivered, is 9.4 per cent, as compared with 14.8 per cent for the entire series. Furthermore, approximately one-half of the 9.4 per cent mortality occurred in the premature group. So we feel that barring accident and interference, there should be a comparatively small mortality in delivering full term babies presenting by the breech.

# RESULTS OF OPERATIONS FOR PROLAPSE OF THE UTERUS AND BLADDER\*

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THIS report is based upon 200 consecutive operations, performed upon 196 patients (Table I) for all degrees of relaxation of the anterior vaginal wall and of prolapse of the uterus.

The results were secured by examination of patients in the hospital Follow-up Clinic and private offices of the operators. Of the 196 patients (Table I), 157 (80 per cent) were followed after operation, the intervals varying from one month to nine years. The percentage of followed patients would have been greater had the study been limited to the years covered by our Follow-up Clinic.

The most important consideration in determining the nature and extent of operative treatment is whether or not the menopause has been passed. As shown in the first table nearly half of the patients had not yet reached the climacteric (Table I).

TABLE I  
OPERATIONS FOR UTERINE AND BLADDER PROLAPSE  
SUMMARY OF FOLLOW-UP

TIME OF OPERATION	TOTAL PATIENTS	NUMBER FOLLOWED
Before Menopause	95	74
After Menopause	101	83
Total	196	157
(Two operations each)	4	4
Total operations	200	
Number followed	161	

## OPERATIONS BEFORE THE MENOPAUSE

*Plastic Operations Alone.*—To avoid possible interference with the childbearing function, we refrained from performing an abdominal sec-

TABLE II  
OPERATIONS FOR UTERINE AND BLADDER PROLAPSE  
BEFORE THE MENOPAUSE  
PLASTIC ALONE

Number of Patients	52
Number Followed	44
Results: Good	32
Improved	6
Incomplete operation	4
Failure	2

\*Read at meeting of the Obstetrical Society of Philadelphia, March 3, 1932.

tion, when a satisfactory result could be expected from plastic work alone, that is to say, when the uterine prolapse was slight and the bladder lesion was of major importance (Table II). Before operating upon such patients the following points should be considered: (1) the amount of lateral and anteroposterior bladder sag; (2) the presence or absence of a low cystocele; and (3) whether there is loss of bladder control from injured or relaxed vesical sphincter.

In treatment of lateral bladder sag, a plication type of operation is usually sufficient. If marked anteroposterior relaxation exists, the bladder is mobilized and sutured to a higher point on the uterus and, when present, the uterine descent is also corrected. The treatment of low cystocele includes a repair of the overlying muscle and fascia and correction of the uterine descent; the latter is accomplished by reefing the cardinal ligaments in front of the cervix. The perineum is always repaired when cystocele operations are undertaken.

Incontinence due to internal sphincter relaxation is treated by plicating the adjacent tissues with mattress sutures, performing the so-called "Kelly operation." Suburethral, hypertrophic, vaginal folds are resected lest the patient assume that the operation was performed incompletely.

Persistent bladder irritability and incontinence were the chief unsatisfactory results following simple, vaginal plastic procedures. We believe that these two symptoms are due to either the recurrence of a small, low cystocele, which results from failure to have shortened the cardinal ligaments, or to inadequacy of the Kelly operation. The finding of the cervix below its normal position after such operative procedures implies imperfect technic. This low position of the cervix, however, may be symptomless because the firm anterior vaginal wall prevents the forward sliding of the urethra, which is the cause of the urinary symptoms.

It is a common observation that bladder irritability may persist for several weeks after a cystocele operation and eventually disappear. Sometimes, however, preoperative and postoperative urinary symptoms are due to obscure neurogenic or intrinsic urinary tract lesions, and are not necessarily due to error in operative technic. Occult spina bifida is a not infrequent example of a neurogenic lesion causing bladder weakness.

*Kelly Operation.*—The Kelly operation (Table III) for relaxation of the sphincter was performed upon 20 of the 196 patients. Of the 5 improved patients (Table III) two had 2 Kelly operations each, one of these two having occult spina bifida with some prolapse had had no childbirth injury. The other patient who required two operations had been incontinent since a forceps injury. In all cases in which the Kelly operation was part of the treatment, the results were better when abdominal suspension of the uterus was combined with the plastic work.



TABLE III  
OPERATIONS FOR UTERINE AND BLADDER PROLAPSE  
BEFORE AND AFTER MENOPAUSE  
KELLY OPERATION

Number of Patients	20
Number Followed	19
Results: Good	12
Improved	5
Failure	2

*Abdominal and Plastic Operations.*—For those patients in the child-bearing age with advanced degrees of uterine prolapse, or with other indications for intraabdominal surgery, some form of uterine suspension, usually by shortening the round ligaments, has been performed, in addition to a repair of the anterior wall and perineum (Table IV). Some form of cervix operation was carried out upon half of the patients falling in this group. An external Alexander operation was performed upon one patient presenting an inguinal hernia. Of the 35 patients in this entire group, 3 required hysterectomy and 5 were otherwise sterilized.

TABLE IV  
OPERATION FOR UTERINE AND BLADDER PROLAPSE  
BEFORE THE MENOPAUSE  
ABDOMINAL OPERATION AND PLASTIC

Number of Patients	35
Number Followed	24
Results: Good	20
Improved	3
Death	1

The results in this whole group were generally satisfactory. The one death in the 200 operations occurred in this group as a result of thyrotoxicosis in a patient who underwent excision of an adenoma of the thyroid gland simultaneously with the prolapse operation.

*Mayo Vaginal Hysterectomy* was performed upon 5 patients suffering from procidentia that required removal of the uterus (Table V). Of the followed cases, the unsatisfactory operative result was an ureteral fistula in a patient with irreducible prolapse.

TABLE V  
OPERATIONS FOR UTERINE AND BLADDER PROLAPSE  
BEFORE THE MENOPAUSE  
VAGINAL HYSTERECTOMY

Number of Patients	5
Number Followed	3
Results: Good	2
Improved	1

*Abdominal Operations Alone.*—Only one patient was treated solely by abdominal operation, shortening of the round ligaments. The result in her case was good.

*Interposition Operations.*—An interposition operation with sterilization was performed on 2 patients approaching the menopause, with a good result in one case and a failure in the other. In the last mentioned case, good result followed a subsequent abdominal operation, which did not present great technical difficulties.

#### OPERATIONS AFTER THE MENOPAUSE

After the menopause the majority of patients were treated by various vaginal operations without abdominal section.

*Plastic Operations Alone.*—Plastic operations alone were done in 39 instances. Of these, the majority were treated by the usual operations on the anterior wall, cervix, and perineum (Table VI).

Vaginal prolapse, following hysterectomy performed elsewhere, was treated by vaginal occlusion with the Le Forte technic in two elderly women. The results were good.

TABLE VI  
OPERATIONS FOR UTERINE AND BLADDER PROLAPSE  
AFTER THE MENOPAUSE  
PLASTIC OPERATION ALONE

Number of Patients		39
Number Followed		30
Results: Good	23	
Improved	6	
Failure	1	

*Vaginal Enterocoele.*—Vaginal enterocoele was the major lesion presented by 3 women who had been operated upon for prolapse in other hospitals. The slight doubt about the diagnosis in these cases was dispelled by finding fat on incising the posterior vaginal wall. Resection of the hernial sac, and a somewhat unsatisfactory suturing of the uterosacral ligaments gave good results.

*Interposition Operations.*—The interposition operation has been the treatment of choice for the large cystocele associated with prolapse of a healthy uterus, if the cervix did not extend much beyond the vaginal introitus (Table VII). When limited to patients in this group, the anatomic and functional results have proved satisfactory. The failure noted in Table VII was a case of complete prolapse; however, a good result followed a subsequent abdominal operation. The imperfect results

TABLE VII  
OPERATIONS FOR UTERINE AND BLADDER PROLAPSE  
AFTER THE MENOPAUSE  
INTERPOSITION OPERATION

Number of Patients		37
Number Followed		33
Results: Good	26	
Improved	6	
Failure	1	

here, as in other methods of treating vesical prolapse, were persistence of bladder irritability, incontinence, or a small, low cystocele. Routinely the fundus was sutured firmly under the pubic rami, and a perineorrhaphy was always done. Our follow-up emphasizes the necessity for dealing with the sphincter relaxation and the low cystocele without depending wholly upon the interposed uterus.

*Vaginal Hysterectomy.*—Vaginal hysterectomy was selected for the treatment of advanced prolapse with ulceration (Table VIII).

TABLE VIII  
OPERATIONS FOR UTERINE AND BLADDER PROLAPSE  
AFTER THE MENOPAUSE  
VAGINAL HYSTERECTOMY

Number of Patients	8
Number Followed	8
Results: Good	6
Improved	1
(Later developed vaginal enterocele)	
No evaluation	1
(Result masked by fixation of vagina due to progressive cancer)	

It is noteworthy that one patient was a nullipara and had carcinoma of the fundus. (One other patient in the "Operations Before Menopause—Plastic Alone" group, developed carcinoma of the cervix several years after operation.)

*Abdominal and Plastic Operations.*—Abdominal and plastic operation, with some form of abdominal wall fixation, was the procedure in 13 patients (Table IX).

TABLE IX  
OPERATIONS FOR UTERINE AND BLADDER PROLAPSE  
AFTER THE MENOPAUSE  
ABDOMINAL AND PLASTIC OPERATIONS

Number of Patients	13
Number Followed	9
Results: Good	8
Improved	1

*Abdominal Operations Alone.*—Abdominal operation alone consisted of fixing the uterus or cervical stump to the abdominal wall in four patients (Table X).

TABLE X  
OPERATIONS FOR UTERINE AND BLADDER PROLAPSE  
AFTER THE MENOPAUSE  
ABDOMINAL OPERATION ALONE

Number of Patients	4
Number Followed	3
Results: Good	3

## COMMENT

At the beginning of the menopause, it is better in some cases to defer operation until the effect of senile changes can be estimated. The operator can then secure better functional results from plastic work.

In the groups in which any one of several methods of fixation of the uterus to the abdominal wall was a part of the treatment of prolapse, the fixation held firmly in all followed patients. Subsequent elongation of the cervix and other forms of prolapse may follow inadequate repair of the pelvic floor.

Pelvic floor repair has been the important feature of treatment in all groups. The results justify the treatment of the majority of cases of genital prolapse after the menopause by vaginal operations, including subvesical interposition and Mayo vaginal hysterectomy.

It is evident that preoperative diagnosis of all the bladder lesions is essential for successful management.

A study of end-results over a sufficient period of time has constantly directed attention to the importance and difficulty of restoring normal anatomic and physiologic conditions in the bladder base and urethra.

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Mayer, A.: Remarks Concerning Thrombosis and Embolism. *Monatschr. f. Geburtsh. u. Gynäk.* 91: 39, 1932.

In Mayer's cases of thrombosis and embolism a decided difference was observed between obstetric and gynecologic patients. In recent years there was no increase in the incidence of these complications among the obstetric patients whereas among the gynecologic patients the incidence of thrombosis increased twofold and that of embolism almost trebled. The cause of this increase is unknown unless it is a change in the constitution of the individual as a result of the mental and somatic changes brought about by the war and the hunger blockade. The gynecologic operations which have a predisposition to be followed by thrombosis and embolism are those for myomas, cancer and prolapse of the uterus.

Two important signs of thrombosis are an inexplicable, persistent tachycardia and above all a slight elevation of temperature. Other signs are swelling of the leg and pain in the sole of the foot.

The danger of embolism is less in cases of manifest than in those of latent thrombosis. The probable cause for this is that in outspoken thrombosis the vein is completely blocked and the blood stream is entirely interrupted whereas in unsuspected cases of thrombosis the blood vessel is not completely obstructed so the blood stream can carry away a piece of the thrombus.

There is no effective prophylactic medication. During the operation prophylaxis consists in control of bleeding, perfect asepsis, and protection of the tissues. After operation, exercise and the administration of large amounts of fluid are helpful.

The treatment of pulmonary embolism depends upon whether there is involvement of the heart, the lungs or the brain. In acute cases morphine may help. Surgical cure should be attempted because the death rate from embolism is very high, but usually there is not sufficient warning to permit a timely operation. In many cases death results from subsequent emboli. Furthermore, among 18 fatal cases of embolism, Dietrich found that the embolus was removable in only seven cases.

J. P. GREENHILL.

## PATHOLOGY OF THE THYROID GLAND COMPLICATING PREGNANCY\*

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**R**ESPONSE by the thyroid gland to physiologic demands and to the exigencies of infection have been observed very frequently. While we have no exact knowledge of the *modus operandi* of the physiologic activity of the thyroid, it seems probable, from observations particularly in regions of endemic goiter, that an insufficient iodine supply will lead to compensatory hypertrophy of the thyroid gland in the course of the ordinary demands of life. Excessive demands, such as pregnancy, may find the gland unable to supply the required amount of thyroxine and hypothyroidism develops. This state, unless severe, may be expected to improve after withdrawal of the added metabolic burden. The goiter so developed will be of the nontoxic diffuse type if the colloid is deposited uniformly or of the nodular type if deposited in a patchy distribution. Recurrent successive stimulations of the former result in a gradual diffuse enlargement, in the latter in coalescence of acini and the formation of adenomas.

In the absence of a deficiency in iodine intake, a perceptible increase in the size of the thyroid gland still can be noted during similar periods of stimulation. Enlargements at puberty, with each menstrual period, and with pregnancy, may be expected. Unlike the gland deficient in iodine, however, the amounts of colloid formed or deposited are not as great, and, these glands return more nearly to their normal size when the stimulation is withdrawn. At times, under these conditions, adenomas may make their beginning but not manifest themselves until later in life.

From the 4000 and upward cases of thyroid disease in the records of the University Hospital, we have selected for the basis of this discussion from a series of 1350 thyroidectomies, 38 patients who developed toxic goiter and 12 who developed simple goiter during pregnancy. The various pathologic conditions of the thyroid gland complicating pregnancy comprise (1) hypothyroidism, (2) simple goiter, (3) toxic goiter, and (4) malignancy of the thyroid.

*Hypothyroidism.*—It does not follow from what has been said above that only those patients in "iodine poor" regions develop hypothyroidism for hardly a day passes in our thyroid out-patient clinic without our seeing patients from this or neighboring seaboard states with some degree of hypofunctioning thyroid glands. Many women with menstrual disorders, familiar to all of you, so commonly associated with hypothy-

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\*Presented, by invitation, before the Obstetrical Society of Philadelphia, March 3, 1932.

roidism, are referred to us for metabolic studies by the Gynecological Clinic. The incidence of sterility is high among hypothyroid women, and it is probably a common experience to find these patients pregnant after the hypothyroidism has been relieved by the administration of thyroid extract. One cannot rely wholly on the basal metabolic rate, especially not on a single estimation, in making the diagnosis of hypothyroidism.

Once pregnancy is established in a woman whose thyroid has proved itself to be incapable of regulating normal metabolic processes, the physician must treat that deficiency. Untreated, the pregnancy is apt to be terminated by miscarriage<sup>1</sup> or if carried to term the child may have cretinism or goiter. Litzenberg and Carey<sup>2</sup> have reported women with hypothyroidism who had previously had several miscarriages, carried to term on adequate amounts of thyroid extract. Results from the administration of thyroid preparations should not be looked for too soon after instituting treatment, nor should one, by forcing these therapeutic agents, try to convert quickly the hypothyroid subject into a normal one. It is better to increase the dose slowly and gradually until the desired effect is obtained.

*Simple Goiter.*—The incidence of simple goiter appearing with pregnancy is variable, and the factors which in our opinion influence the incidence, are locality and the time of appearance of the various reports with relation to the introduction of the use of iodine in the treatment of goiter. The appearance of simple thyroid enlargement during pregnancy has been noted for many years. It is to be expected that in regions where endemic goiter is prevalent that the incidence would be much higher than in this locality. Yoakum<sup>3</sup> and Davis<sup>4</sup> report that in such regions as high as 40 per cent to 60 per cent of pregnant women develop simple goiters. Simple enlargements of the thyroid gland during pregnancy in this locality in the majority of cases quickly subside after delivery. If goiter persists, it rarely impairs the future health of the mother though with successive pregnancies, the goiter may increase in size. Tait<sup>5</sup> first called attention to this phenomena over fifty years ago though since the widespread use of iodine as a prophylaxis against goiter it has not been so frequent. The subsequent enlargement of simple goiter of the colloid type during pregnancy can be prevented by the administration of iodine. In this connection, a word of caution about the indiscriminate use of iodine may be spoken. There is evidence to show that simple, nontoxic, nodular (adenomatous) goiters may be rendered toxic by its use. The number of women requiring thyroidectomy for simple goiter during pregnancy is extremely small. If pressure symptoms threaten the life of the mother, thyroidectomy can be done with safety under local anesthesia. We think it is significant that only 12 of our 1350 women required partial thyroidectomy for a simple goiter which appeared during an earlier pregnancy. No operation was required during the pregnancy in which the goiter appeared, several

months to many years intervening. Eight of the women had had from one to seven pregnancies between the appearance of the goiter and operation, and of these only three were definitely of the opinion that there had been successive enlargements with successive pregnancies. Eleven of the mothers were delivered of normal babies at the end of the pregnancy, during which the goiter appeared; one miscarried as she did again before operation, for a cause undetermined during the period of our observation. She was not hypothyroid. From these observations it can be said that the rôle of simple goiter as a complication of pregnancy is unimportant.

*Toxic Goiter.*—Thyrotoxicosis in either of its clinical forms, toxic nodular goiter, or toxic diffuse goiter, presents such a variety of symptoms and signs, that frequently it masquerades under the wrong diagnosis and too often is improperly treated. Chief among these erroneous diagnoses are nervous breakdown, heart disease, and some disease of the gastrointestinal tract. Before considering the bearing of thyrotoxicosis upon pregnancy, a word as to the diagnosis. At times the diagnosis is by no means easy or obvious. Nervousness, both subjective and objective, is a frequent accompaniment of the state of pregnancy. Tachycardia is by no means uncommon during pregnancy. Though it is unlikely that obstetricians would mistake the gastrointestinal manifestations of hyperthyroidism for those which frequently accompany pregnancy, the recent contribution by Falls<sup>6</sup> on the use of Lugol's solution in hyperemesis gravidarum is pertinent. He says "certain patients who have died with the clinical picture of hyperemesis gravidarum, have presented a similar picture to that of thyrotoxicosis" and some patients, who had been desperately sick with hyperemesis gravidarum during a given pregnancy were kept free of that complication during successive pregnancies by the administration of Lugol's solution. The incidence of thyroid enlargement during pregnancy has already been mentioned and when present in association with nervous phenomena, tachycardia, and gastrointestinal disturbances, the diagnosis of toxic goiter may be made too quickly. It is well known that during pregnancy, particularly in the latter months, the basal metabolic rate rises. Plass and Yoakum<sup>7</sup> concluded from their observations of 72 women that the basal metabolism during a normal, uncomplicated pregnancy, increased approximately 15 per cent, with a fall to normal in the first few days after delivery. The mechanism of this increase has been explained in the excellent papers by Sandiford and Wheeler<sup>8</sup> and Boothby and Sandiford<sup>9</sup> who presented complete data on respiratory metabolism. They found that the total calories for each hour were 25 per cent greater in the last months of pregnancy than before conception. Their calculations indicated that the increased metabolism was due to the increased protoplasmic mass.

There are various quotations as to the incidence of hyperthyroidism in pregnancy or pregnancy in hyperthyroidism. Yoakum reported

nearly a thousand cases of pregnancy without the association of hyperthyroidism in any. Mussey, Plummer, and Boothby<sup>10</sup> showed the incidence of pregnancy in hyperthyroidism to be 0.6 per cent, and Clute and Daniels<sup>11</sup> at the Lahey Clinic found it to be 0.41 per cent. In our records, we found 44 patients, or 3.2 per cent, in whom thyrotoxicosis began during pregnancy; 21 of these had toxic nodular goiter and 23 toxic diffuse goiter. Of the latter, 7 had thyroidectomy during their pregnancies. The infrequency of associated hyperthyroidism and pregnancy is at once apparent.

Apart from the incidence, we are more concerned with the influence of pregnancy upon hyperthyroidism and the effect of hyperthyroidism upon pregnancy. Clute and Daniels found nothing unusual among their cases of hyperthyroidism in pregnant as compared with nonpregnant women. Multiple stage thyroidectomies were no more frequent in one group than the other. In 68 of 112 cases reported by Seitz<sup>12</sup> the hyperthyroidism was definitely aggravated by pregnancy, 11 had premature labors, 5 miscarried, and 7 died. Following the course of 31 pregnancies in 17 women with hyperthyroidism, Gardiner-Hill<sup>13</sup> felt that the thyrotoxicosis was not made worse by the pregnancies, though in his series there were two stillbirths, eight premature births, and nine miscarriages. Neither did Hyman and Kessel<sup>14</sup> find that pregnancy made the thyrotoxic mothers worse. Nine of their patients had eleven normal children and one stillbirth. Mussey, Plummer, and Boothby agree that thyrotoxicosis is not appreciably influenced by pregnancy. Falls says that if toxic symptoms are present before conception, they are usually aggravated but may be ameliorated by pregnancy. The latter occurred in one case reported by Mussey and Plummer and in one of our patients, though six months later her thyrotoxicosis was reactivated and required a thyroidectomy.

In the collected cases of Gardiner-Hill one-half of the pregnancies terminated either in abortion or premature delivery. In eight of his own cases of primary Graves' disease, developing during pregnancy, there was one full-term stillborn baby and one miscarriage at three months. On the other hand, of the 38 mothers with hyperthyroidism in the series of Mussey and Plummer, 37 were delivered of 36 normal children, including one set of twins and one premature living child. One stillbirth followed forceps delivery.

In our own series, of 38 women who developed toxic goiter during their pregnancies (but who were operated upon by us from several months to several years after delivery), there was but one miscarriage. Eleven of these 38 women had additional pregnancies between the time during which thyrotoxicosis developed, and the date of the thyroidectomy. Four of the mothers had one additional normal pregnancy, two had two, and one had three. Two had one normal pregnancy followed by a miscarriage, one had one miscarriage, and one had three miscarriages.



It is quite improper to draw any statistical conclusions from these quotations since there must be many cases of thyrotoxicosis in pregnant women that are not recorded in the thyroid clinics.

We wish now to present the records of seven patients with toxic diffuse goiters upon whom a thyroidectomy was performed during their pregnancies.

CASE 1.—P. L., aged twenty-two, married, housewife, primipara. Thyrotoxicosis began in 1924. Goiter and exophthalmos appeared in June, 1925. Nervousness, loss of weight, increasing muscular weakness, and marked palpitation were complained of on her first admission to the medical wards of the University of Pennsylvania Hospital in January, 1926. She had taken Lugol's solution for one month prior to admission. Basal metabolic rate was plus 61. She had several series of radium treatments and Lugol's solution intermittently during the next nine months. She was transferred to the surgical service in November, 1926, at which time a right lobectomy was performed. After discharge she became pregnant, in the second month of which she was readmitted to the surgical service for a left lobectomy. Basal rate was plus 70 on this admission. Left lobectomy was performed in February, 1927. Ten weeks later her basal metabolic rate was plus 4. When seen in the eighth month of her pregnancy there was no clinical evidence of toxicity. A normal, healthy baby was delivered at term. She remained so well after delivery that she refused to return for follow-up until ten months after delivery at which time basal rate was plus 8.

CASE 2.—E. W., aged twenty-five, married, housewife, primipara. In November, 1924, she had a series of boiling water injections into the thyroid, then bipolar ligations for toxic diffuse goiter. In May, 1925, subtotal thyroidectomy was performed while the patient was four months pregnant. A normal healthy baby was delivered in November, 1925. She remained perfectly well after delivery until January, 1927, when she developed a recurrence of thyrotoxicosis. She was reoperated upon in July of that year. She was seen at the follow-up clinic four times in the next twenty-one months. At no visit was there any evidence of toxicity.

CASE 3.—H. S., aged twenty-three, married, housewife, primipara. Symptoms of thyrotoxicosis began eighteen months before admission in October, 1927. Exophthalmos had been present for three months. She had taken Lugol's solution for ten months before admission. Basal metabolic rates while in the hospital before operation were plus 66, 62, and 58. She was in the fourth month of her pregnancy. Subtotal thyroidectomy was performed. Basal rates before discharge were plus 33 and 32. Five weeks later basal rate was minus 1, pulse 72. Full term, normal, healthy baby was born in March, 1928. In February, 1929, she reported that she was perfectly well. In March, 1930, her basal rate was plus 7, pulse 72, her exophthalmos was gone, and we considered her entirely well.

CASE 4.—D. H., aged twenty-three, married, housewife, para iii. During her second pregnancy, eighteen months before admission in May, 1929, symptoms of hyperthyroidism had appeared along with thyroid enlargement. Exophthalmos was first noted in January, 1929, following influenza. Basal metabolic rates in the hospital were plus 70, plus 54, and after thirteen days of Lugol's solution, plus 42. After subtotal thyroidectomy and before discharge, her basal rate was plus 30. Seven and a half months after operation she delivered a full-term healthy baby. This pregnancy was the easiest of her three. She felt so well during and after pregnancy that our first follow-up was thirteen months after operation, at which time we first found out that she had been pregnant at the time of thyroidectomy. In May, 1931, her basal rate was plus 16, pulse 72, she had no subjective or objective nervousness, did her usual work without fatigue and felt perfectly well.

CASE 5.—H. M., aged twenty-two, married, factory worker, primipara. First presented herself to our thyroid out-patient clinic in June, 1930, when a diagnosis of toxic diffuse goiter was made. She had had symptoms of toxicity for six months previously. Her basal rate was plus 48. After having been on Lugol's solution for ten days at another hospital, she was admitted to our service July 21, 1930, with a basal rate of plus 16. She was then entering the second month of her pregnancy. Three days after admission a subtotal thyroidectomy was performed. At discharge her basal rate was plus 6. In January, 1931, there was no clinical evidence of toxicity. In February, or the eighth month of her pregnancy, her basal rate was plus 1, pulse 88. Healthy, full-time baby was born March 10. The mother was last seen in November, 1931, when her basal metabolic rate was plus 14 and we considered her perfectly well.

CASE 6.—F. K., aged thirty-four, married, housewife, para iii. Symptoms of thyrotoxicosis began two years before admission following a ruptured ectopic pregnancy. Six months after onset, a goiter appeared. She was admitted to the hospital May 18, 1931, with a basal metabolic rate of plus 38. She had a definitely hyperplastic gland, exophthalmos, hyperidrosis, and tachycardia and tremors. Her last period had been on December 9, 1930. A chronic, bronchial asthma had become much worse since her pregnancy began. Subtotal thyroidectomy was performed on May 27, 1931. At discharge her basal rate was plus 2. Her pregnancy continued uninterrupted to full term, her baby being born September 16, 1931. She returned for follow-up this February, when her basal rate was plus 3, and she showed no evidence of toxicity.

CASE 7.—E. F., aged thirty-three, married, housewife, para iii. Her last regular period was January 14, 1931. Her pregnancy was uneventful until late in April when she developed symptoms and signs of toxic diffuse goiter. On May 16, 1931, she was admitted to the hospital. Lugol's solution, minims 30 daily, started at once, adequate sedatives and rest in bed, except for bathroom privileges, was the program. Her pulse rate was 160. After being on Lugol's solution for one week her basal metabolic rate was plus 40. Five days later it dropped to plus 24. On June 2, 1931, a subtotal thyroidectomy was performed. Her convalescence was uneventful as was the remainder of her pregnancy which ended at full term in the delivery of a normal baby. When seen March 2, 1932, her pulse was 88, and she had no clinical evidence of thyrotoxicosis. Her basal rate was plus 24, but she had a cold and had driven her car 30 miles (after a four hour sleep the night before) to come for the test. She feels perfectly well.

This is an impressive and convincing demonstration and forces us to the conclusion that patients with toxic goiter complicating pregnancy tolerate thyroidectomy as well as those not pregnant. All of the children of these mothers were normal and healthy.

Recurrences or relapses after thyroidectomy does occur in a small percentage of cases, but in none of 28 of such cases in our clinic was recurrence caused by pregnancy. We occasionally have the opportunity in the two-year follow-up period after thyroidectomy of observing the course of pregnancy. A brief synopsis of three such cases follows:

CASE 8.—M. H., aged twenty-eight, developed thyrotoxicosis during her first pregnancy which terminated normally in December, 1928. All symptoms were aggravated during lactation. Despite iodine therapy and maximum rest, she came to us for thyroidectomy in April, 1930. Basal metabolic rate was plus 34. Subtotal thyroidectomy was performed May 3, 1930. Basal rate on May 14 was plus 6. In October, 1930, she returned for follow-up being four months pregnant. Her basal

metabolic rate was minus 11, pulse 72, and blood pressure 102/56. On March 26, 1931, a normal, full-term living child was born. She reported that her pregnancy had been entirely uneventful. We last saw her in May, 1931, when we agreed with her that she was perfectly well. Her basal metabolic rate was minus 6, pulse 76.

CASE 9.—W. W., aged twenty-five, had had a right lobectomy and left superior polar ligation for toxic diffuse goiter at another hospital four years before coming to us. She was frankly toxic on admission to our service on May 1, 1930. Basal rate was plus 54, pulse 140. After preparation with iodine, a left lobectomy was performed on May 8. Basal rate on the sixth day postoperative was plus 20. In September, 1930, her pulse was 80 and basal rate plus 15. There was no clinical evidence of toxicity. In May, 1931 she was in the seventh month of her pregnancy. Basal metabolic rate was plus 32, pulse 84. The clinical evidence did not substantiate the basal rate. In September, 1931, when last seen, she reported that her pregnancy had proceeded uneventfully to term when a normal, healthy baby was born in July. In September, 1931, her basal rate was plus 3 and pulse 84.

CASE 10.—C. C., aged thirty-eight, had subtotal thyroidectomy for toxic diffuse goiter in October, 1930. In May, 1931, basal metabolic rate was plus 5, pulse 82. She was then two months pregnant. In September, 1931, blood pressure was 140/70, pulse 90, basal metabolic rate plus 19. We considered her mildly thyrotoxic and started Lugol's solution, minims 3 daily. She was last seen February 3, 1932, nearing the eighth month of her pregnancy. Blood pressure 125/70, pulse 96, basal rate plus 21. She had no tremors; there was no demonstrable evidence of toxicity, and she denied any subjective nervousness. She was instructed to continue on iodine until after delivery.

It appears from our experience and that of others, that pregnancy is not a factor in the production of recurrent thyrotoxicosis. In the series of Clute and Daniels 53 women who had had thyroidectomy for thyrotoxicosis bore 69 children subsequent to operation, with only one developing what might have been recurrent toxicity. If evidence of toxicity does develop during pregnancy, the judicious use of iodine probably will carry the mothers safely to term, when the symptoms will subside by virtue of their being relieved of the added metabolic burden.

Having reviewed in our experience and the experiences of others the incidence of toxic goiter complicating pregnancy and the effect of toxic goiter upon the outcome of pregnancy, the question of importance alike to obstetrician and surgeon is this: under what circumstances should surgical treatment be considered appropriate, or, if you choose, imperative when thyrotoxicosis complicates pregnancy? Perhaps we should preface our answer to this question by a statement as to the termination of pregnancy. Are there any circumstances under which pregnancy should be terminated because of thyrotoxicosis? In several of our cases this had been seriously considered before we had been called in consultation. There may be aggravated forms of toxicity, in which such a course might seem desirable; if so, we have not seen them. And we would like to record our opinion in emphatic terms that the termination of pregnancy should be discountenanced. Let us remind you that in our series of thyroidectomies in pregnant women there were no fatalities and the mothers were delivered of normal babies.

As for the indications for the surgical treatment of toxic goiter in

pregnancy, one should be influenced wholly by the degree of toxicity. In toxicity of mild degree, we advocate a trial course of iodine. If the toxic symptoms subside altogether, or are kept under reasonable control, the question of operation may be deferred until after delivery. But, be it remembered that patients whose toxicity during the early months of pregnancy has been controlled by iodine, may become iodine fast and get out of control toward the end of pregnancy. Thyroid crises occasionally develop with alarming rapidity even while the patients are being properly treated. If the toxicity is not favorably influenced by iodine, if the toxic state persists or becomes aggravated, a thyroidectomy offers the best prognosis for both mother and child. We have had no cases of abortion. In pregnancies that follow thyroidectomy, the obstetrician should be on the look-out for the slightest suggestion of a relapse and at once institute iodine therapy.

As to the time at which the operation should be performed, that is, whether in the early or late months of pregnancy, one should not be influenced by the pregnant state but by the degree of toxicity. As a matter of fact, in our decisions for or against operation, we have, except in the milder forms of toxicity, disregarded the pregnant state altogether and considered the patient only as a subject of thyrotoxicosis. The likelihood of the degree of toxicity becoming more advanced as the pregnancy advances, has prompted us to advise operation once the diagnosis is established.

*Malignancy of the Thyroid.*—Carcinoma and sarcoma of the thyroid gland are not uncommon. Two per cent of all the nodular goiters removed at the University Hospital have been malignant. The early diagnosis of malignancy of the thyroid is difficult and too often it goes unrecognized until it is too late to cure the patient. Our experience with carcinoma of the thyroid occurring in a pregnant woman is limited to the case summarized here.

CASE 11.—M. P., aged thirty, married, white woman, para ii. During her first pregnancy in 1929, she developed a unilateral nodular enlargement of the thyroid gland. Her pregnancy terminated normally with the birth of a healthy, normal child. The thyroid enlargement gradually disappeared after delivery. In March, 1931, when the patient was entering the second month of her second pregnancy, the goiter reappeared. Until June the tumor was slow growing. From then on its growth was rapid and soon produced a severe hacking cough with dyspnea on exertion. Because of these complaints, the patient was admitted to the Medical Service of the University Hospital, July 22. On admission she was orthopneic, slightly cyanosed about the face and neck, had "crowing" respirations, and was in great distress. There was a large visible mass in the lower part of her neck. She was then entering the sixth month of her pregnancy.

Roentgenogram of her neck and chest showed an enormous thyroid encroaching upon the lumen of the trachea with a large, substernal mass. Bronchoscopic examination revealed displacement and compression stenosis of the trachea, also a small fungating mass of tissue in the trachea.

The patient was transferred to our service on July 30, 1931. The following day we operated upon her. A huge tumor mass was found filling the neck. Neither the

lateral nor the inferior limits of the tumor could be determined. A piece of the tumor the size of an orange, was removed from over the trachea. The thyroid isthmus was resected. These procedures bared the trachea for a distance of 2 cm.

The patient convalesced satisfactorily and was discharged August 10 after receiving the first of a series of x-ray treatments over the tumor. She received x-ray treatments again on August 12 and August 14. On August 16, because of urgent dyspnea she was admitted to the Bronchoscopic Service where tracheotomy was performed. Again after discharge intensive x-ray treatments were continued.

Despite these events, her pregnancy continued to term. On November 30, 1931, a normal living child was delivered. The mother was still under treatment by the X-ray Department. When last seen she was quite comfortable with the tracheotomy tube still in place. The tumor mass in her neck was considerably smaller than it was on her discharge from the hospital.

The treatment of malignancy of the thyroid must be radical. When the neoplasm appears to be confined to one lobe, complete lobectomy and excision of adjacent lymph nodes, infiltrated fascia and muscles should be followed by x-ray therapy. When complete excision cannot be done, relief from or prevention of tracheal compression should be the aim of whatever operation is attempted. Baring the trachea greatly facilitates tracheotomy should such become necessary. The presence of the state of pregnancy, associated with malignancy of the thyroid gland, does not alter our program of partial or complete excision of the tumor followed by x-ray therapy.

#### SUMMARY AND CONCLUSIONS

1. An appreciable response by the thyroid gland to the state of pregnancy is frequently noted.

2. Hypothyroidism in a pregnant woman may cause miscarriage; or if a living baby is delivered, the baby may have cretinism or a goiter. The judicious administration of thyroid extract to pregnant, hypothyroid mothers will prevent these complications.

3. The development of simple goiter during pregnancy usually does not interfere with the normal course of events and does not affect the child. The use of iodine during pregnancy may prevent the development of simple goiter.

4. Nodular goiters, which by their size or location, threaten the life of the mother by pressure on the trachea and recurrent laryngeal nerves, should be removed regardless of pregnancy.

5. Thyrotoxicosis developed during pregnancy in 3.2 per cent of the women upon whom thyroidectomy has been performed in our clinic.

6. The records of seven patients with toxic goiter, upon whom thyroidectomy was performed during their pregnancies, are reported. All of the pregnancies went to term and the mothers were delivered of normal babies.

7. Pregnancy should not be voluntarily terminated because of the development of thyrotoxicosis.

8. Mild degrees of thyrotoxicosis during pregnancy may be controlled by the use of iodine.

9. In cases where severe degrees of thyrotoxicosis complicate pregnancy or in milder degrees of toxicity not controlled by iodine, thyroidectomy should be performed at once.

10. The recurrence of thyrotoxicosis during pregnancy, subsequent to thyroidectomy for toxic goiter, may be prevented by the administration of iodine.

11. The treatment of malignant tumors of the thyroid should be carried out without regard for an associated pregnancy.

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(For discussion, see page 941.)

## UNCOMPLICATED PROLAPSE OF THE OVARY, DUE TO ELONGATION OF THE INFUNDIBULOPELVIC LIGAMENT, AND ITS TREATMENT\*

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THERE are some conditions in gynecology, probably in other branches of medicine as well, that are apparently ignored or forgotten periodically, although known for a considerable time. This is true of uncomplicated prolapse of the ovary, unassociated with displacement of the uterus, pelvic inflammation or other pelvic pathology.

It was discussed by Rigby as long ago as 1850, by the members of the Boston Gynecological Society in 1872; was noticed by Skene in 1878, by Paul Mundé in 1879. Imlach in 1886 advocated the suture of the hilum of the ovary to the relaxed infundibulopelvic ligament near the brim of the pelvis and called it oöphororrhaphy. Saenger's notable article on the subject in 1896, like so much that Saenger did, established the condition on a scientific basis as to its etiology and proposed for the first time a logical treatment. The following year prolapse of the ovary, with a suggestion for its treatment, formed part of a contribution to the transactions of the Gynecological Section of our College of Physicians. Of the four cases reported at that time one of the patients had been operated upon two years before by a procedure very much like that of Saenger's but independently as the operation had been done a year before the appearance of his paper. The latter had in his first operation passed a stitch through the ovarian fimbria and the same thread through a fold of the peritoneum over the infundibulopelvic ligament, tying the two ends of the thread together, thus shortening the ligament. The contributor to the Gyneco-

\*Read at meeting of the Obstetrical Society of Philadelphia, March 3, 1932.

logical transactions had caught the infundibulopelvic ligament just at the outer edge of the ovary and had then passed the stitch through a fold of peritoneum and pelvic fascia in front of the iliac vessels, thus practically obliterating the suspensory ligament of the ovary, a procedure since modified and improved.

In 1903 Mauclore proposed an operation for prolapse of the ovary by button-holing the broad ligament below the round ligament, passing the ovary through the opening after cutting the ovarian fimbria and fastening it on the anterior face of the broad ligament by two stitches, one at each end of the ovary. Then if the patient desired children the fimbriated extremity of the tube was fastened in immediate proximity to the ovary.

Barrows, in the *Medical Record* of October, 1904, proposes the same procedure except that he passes the ovary through the broad ligament above instead of below the round ligament. Barrows did his first operation in 1901, two years before Mauclore published the account of his. In 1907, George Gray Ward advocating Barrow's procedure, gives an extensive and interesting review of the subject. In the course of this review he expresses surprise that there are specialists who entirely ignore the condition and quotes one man of reputation who confesses entire ignorance of the subject. Ward might have been still more astonished at Stoeckel's recent statement (1928) that the whole thing was nonsense; ("Die Ovariopexie ist ein Unsinn") a rather summary dismissal of a matter that has interested many men of large experience, more than average powers of observation and good judgment.

In 1909 Stratz published an interesting paper on all the displacements of the ovary, reporting five cases of forward displacement and quoting Sellheim's 44 cases of upward displacement (imperfect descensus). Stratz's proposition for the correction of too wide an excursion of the ovary from its normal position is to fasten both ends of it to the round ligament, a proposition, to judge from one of his pictures, based on the mistaken supposition, we believe, that the displacement of the ovary is due to abnormal elongation of the ovarian ligament.

Reiffersheid in 1924 dismisses the treatment of prolapsed ovary with the statement that Saenger's ovariopexie must very rarely be required. Kelly in 1928 acknowledges the importance of the condition and gives a good description of the symptoms, but proposes plicating the uterosacral ligaments to reform a fossa ovarica in which the ovary may rest and advocates shortening the tuboovarian ligament. Neither of these procedures, in our judgment, would correct a descensus ovarii. Von Jaschke in 1929 states that only very rarely would the Saenger operation be indicated. And finally the book on *Gynäkologische Operationslehre* by Peham and Amreich, published in 1930 says nothing about it.

The occurrence of simple, uncomplicated prolapse of the ovary is rare, is not always provocative of troublesome symptoms and moreover it may occur and recur at varying intervals, the ovary meanwhile occupying a normal position. We have had an opportunity to observe this phenomenon in several instances. For example in a multipara, in consequence of manual reposition, tampons, knee chest posture and the temporary use of a pessary, the ovary would remain in good position for a time. Then, suddenly, the ovary would prolapse to the bottom of Douglas' pouch. The patient was immediately aware of what had happened; became nauseated, incapacitated and had to be sent home in a cab. In another patient, a young nullipara under observation for a couple of years, the ovary, at first totally prolapsed, had remained in good position after manual reposition for nine months when, on alight-

ing from a street car, the prolapse suddenly recurred with its distinctive symptoms. Both these patients were permanently relieved by the operation described as the first procedure presented to the Gynecological Section of the College.

In addition to this peculiarity in its symptomatology of sudden occurrence and recurrence, with nausea and disability, there is often, as might be expected, extreme pain on defecation and dyspareunia.

Of late years the operation first described by us has been modified and simplified. It now consists simply of three insertions of the threaded needle directly under the infundibulopelvic ligament: one next to the ovary, one in the middle of the ligament and one at its pelvic extremity, avoiding the blood vessels. By tying the ends of the suture together the whole length of the ligament disappears, or by making the last insertion of the needle a little short of the pelvic end of the ligament a sufficient reduction of its length is secured to bring the ovary to a normal level.

It appears from this technic that we accept Saenger's explanation for prolapse of the ovary: That it can be due only to an abnormal length of its suspensory ligament. In addition to its employment for ovarian prolapse per se, we find this operative procedure of use when operating for retrodisplacement of the uterus or after salpingectomy for pelvic infection. For if an elongated infundibulopelvic ligament is overlooked and one may be three times or more the length of its fellow, or both may be abnormally lengthened, then the patient, relieved of her major pelvic pathology, may subsequently suffer from the disagreeable symptoms of ovarian prolapse.

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(For discussion, see page 942.)



## REVIEW OF 570 FORCEPS OPERATIONS\*

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**D**ELEE states that "the forceps of obstetrics is an instrument designed to extract the fetus by the head from the maternal passages, without injury to it or to the mother. As soon as the right of either is encroached upon, the instrument ceases to be the forceps of obstetrics but becomes simply an instrument of extraction, similar to the craniotomy forceps and not so good."

✓ The incidence of instrumental delivery in recent years has grown so enormously that a glimpse at the White House Conference Questionnaire concerning deliveries during 1929 might not be out of place. Two hundred and seven general hospitals reported 120,999 deliveries with 21,097 forceps, or 17.4 per cent; 16 obstetric clinics reported 24,813 deliveries with 5,075 forceps, or 20.4 per cent. Taken together there were 145,812 deliveries with 26,172 forceps, or 17.9 per cent, an incidence of one forceps operation in every 5 or 6 deliveries. | If forceps were applied where actually needed, a figure of not over 5 per cent should represent the incidence of its use.

( The group of cases which it is my privilege to present consists of 570 forceps deliveries occurring in a series of 16,442 cases, covering a period of approximately ten years, delivered on the University of Maryland indoor and outdoor services and the Health Department Obstetrical Service.

Number of deliveries ..... 16,442  
 Number of forceps ..... 570 (1 in 29)  
 High 63, Mid 229, Low 278.

### INDICATIONS

#### High Forceps:

Contracted pelvis	22	Face presentation	3
Posterior occiput	13	Aftercoming head	2
Transverse arrest	7	Prolonged labor	2
Fetal distress	5	Placenta previa	1
Prolapsed cord	4	Antepartum eclampsia	1
Maternal distress	2	Not stated	1

#### Mid Forceps:

Posterior occiput	70	Abruptio placentae	5
Prolonged labor	48	Maternal heart disease	5
Fetal distress	35	Maternal tuberculosis	1
Contracted pelvis	26	Aftercoming head	1
Transverse arrest	14	Face presentation	1
Maternal distress	9	Prolapsed cord	1
Eclampsia	8	Not stated	5

#### Low Forceps:

Prophylactic	141	Transverse arrest	5
Prolonged labor	46	Maternal distress	2
Fetal distress	30	Face presentation	2
Posterior occiput	25	Pneumonia	2
Eclampsia	12	Abruptio placentae	1
Prolapsed cord	6	Placenta previa	1
Maternal heart disease	5		

\*Read before the Obstetrical and Gynecological Section of the Baltimore City Medical Society, January 15, 1932.

## SUMMARY OF INDICATIONS

Prophylactic	141	Maternal heart disease	10
Posterior occiput	108	Face presentation	6
Prolonged labor	96	Abruptio placentae	6
Fetal distress	70	Aftercoming head	3
Contracted pelvis	48	Placenta previa	2
Transverse arrest	26	Maternal tuberculosis	1
Eclampsia	21	Pneumonia	2
Maternal distress	13	Not stated	6
Prolapsed cord	11		

TABLE I. MATERNAL MORTALITY AND MORBIDITY

<i>High Forceps:</i>			
Mortality	0	0.0	per cent
Morbidity	15	23.8	per cent
Sufficiently severe to require more than two weeks in hospital 5, 7.93 per cent			
<i>Mid Forceps:</i>			
Mortality	3	1.31	per cent
Eclampsia	1		
Eclampsia with pneumonia	1		
Puerperal infection	1		
Morbidity	54	23.58	per cent
Sufficiently severe to require more than two weeks in hospital 11, 4.80 per cent			
<i>Low Forceps:</i>			
Mortality	7	2.51	per cent
Cardiac (on table)	2		
Acute toxemia	1		
Acute yellow atrophy	1		
Eclampsia	3		
Morbidity	54	19.40	per cent
Sufficiently severe to require more than two weeks in hospital 21, 7.55 per cent			
Total maternal mortality	10	1.76	per cent
Total maternal morbidity	123	21.57	per cent
Sufficiently severe to require more than two weeks in hospital			
	37	6.66	per cent

The following is a brief résumé of the fatal cases:

## MID FORCEPS

Case 1.—Colored primipara aged fifteen years, a service case. Physical examination negative and pelvic measurements normal. This patient had a prolonged first and second stage of labor. The fetus presented as an occipitoposterior. A double application of forceps was done and a stillborn child delivered. Following delivery the mother developed a very severe postpartum infection and died.

Case 2.—Colored primipara aged twenty years, a service case, with a diagnosis of antepartum eclampsia. The pelvis was generally contracted with an external conjugate of 18 cm. An occipitoposterior presentation was diagnosed and the patient was delivered by a mid forceps operation. Following delivery the patient continued to have convulsions and in a short time developed pneumonia and after remaining in the hospital for twenty-nine days, she died.

Case 3.—Colored para iii aged twenty-eight years, a service case, with a diagnosis of antepartum eclampsia. The patient had previously delivered twice normally. Her pelvic measurements were normal. The patient went into labor and her convulsions continued. A mid forceps operation was performed and a stillborn infant weighing 8 pounds was delivered. This child was the first of twins. The second baby was delivered as a breech presentation. The patient died thirty hours after admission to the hospital, her temperature going as high as 110° F.

## LOW FORCEPS

Case 4.—White primipara, twenty-two years, service case. Physical examination was unsatisfactory because the patient was comatose on admission. Delivered by low forceps of a child weighing 1450 gm. Shortly after delivery the patient died, and at autopsy a diagnosis of acute yellow atrophy of the liver was made.

Case 5.—Colored para ii, aged twenty-eight years, a service case. The patient had been delivered previously by means of forceps of a living child. Her pelvic measurements revealed a generally contracted pelvis with an external conjugate of 18 cm. A stillborn child was delivered with low forceps, the head presenting as an R. O. P. While the patient was being delivered she suddenly ceased to breathe, death being due either to a cardiac condition or to the anesthetic.

Case 6.—White primipara aged twenty, a private case with a history of having had twelve antepartum convulsions. The patient was treated conservatively and allowed to go into labor. When the labor was almost terminated a low forceps operation was performed and a stillborn child delivered. The eclamptic attacks continued until the patient died. No anesthetic was used.

Case 7.—Colored primipara aged twenty-three, a service case, with a history of having had four antepartum convulsions. The patient was in deep coma on admission, and it could be seen that she would cease to breathe very shortly. A thirty-six weeks' macerated fetus was delivered with low forceps without an anesthetic, and the patient died while being delivered.

Case 8.—Colored para vi, aged thirty-two, a service case. Her pelvic measurements were normal. The patient was admitted in extremis with a temperature of 103° F., a pulse of 160 per minute and respirations 52 per minute. Fetal heart not heard on admission. Her first and second stages of labor had been prolonged, the patient was delivered without an anesthetic with low forceps of a stillborn child weighing 8½ pounds. A diagnosis of obscure acute toxemia was made. Autopsy was not obtainable. The patient died shortly after admission.

Case 9.—White primipara, aged nineteen, a service case, with a history of having had several antepartum eclamptic attacks. External conjugate 18 cm. The patient was treated conservatively, and when the head reached the perineal floor, a low forceps operation was performed and a stillborn child weighing 4 pounds 14 ounces was delivered. The eclampsia continued and the patient died in spite of treatment.

Case 10.—Colored para x, aged thirty-eight, a service case. Her pelvic measurements were normal and she had previously been delivered normally 5 times and by forceps 4 times, a living child having been obtained in each instance. This case was very similar to Case 5. An easy low forceps operation was performed and a child weighing 9 pounds 13 ounces was delivered through a very relaxed outlet. While the patient was being delivered, she ceased to breathe, and death was probably due to either a cardiac condition or to the anesthetic.

The mortality and morbidity figures given above represent the total uncorrected results. The morbidity figures reported are based upon temperatures taken every four hours and any elevation above 100.4° F. for two successive days placed the patient in the febrile group. It can be seen that the majority of the patients in this group were discharged from the hospital within two weeks after delivery, a special classification having been made for those patients requiring more than two weeks' hospitalization. Any attempts at giving corrected mortality and morbidity figures are always filled with danger. For example, of the three mothers who died in the mid forceps group, the two cases of eclampsia might very

well be omitted from so-called forceps deaths, leaving only the death from puerperal infection attributable to this operation. This would give us a corrected maternal mortality for mid forceps of 0.40 per cent. Considering the low forceps groups in the same manner, the cases of acute toxemia, acute yellow atrophy and eclampsia not being directly attributable to the forceps operation, there remain only the two patients who died on the table, either from a cardiac condition or as anesthetic deaths. This would give us a corrected mortality for low forceps of only 0.70 per cent.

If we were to consider the case of the patient who died of puerperal infection following a mid forceps operation as the only death attributable to the operation itself, the corrected maternal mortality would be 0.176 per cent, and if we were to include the two patients who died on the delivery table of either a cardiac condition or because of the anesthetic, the corrected maternal mortality would be 0.53 per cent.

TABLE II. RESULTS TO CHILD

	STILLBORN		DYING IN TWO WEEKS
	22, 34.9 %		6, 9.52 %
<i>High forceps: (63)</i>			
Intracranial hemorrhage	7	Intracranial hemorrhage	5
Intrauterine asphyxia	5	Hemophilia	1
Maternal toxemia	3		
Prolapsed cord	3		
Abruptio placentae	2		
Placenta previa	1		
Macerated	1		
<i>Mid Forceps: (229)</i>	28, 12.22 %		18, 7.86 %
Intrauterine asphyxia	16	Intracranial hemorrhage	11
Intracranial hemorrhage	4	Prematurity	5
Maternal toxemia	3	Intrauterine asphyxia	1
Macerated	3	Congenital atelectasis	1
Prolapsed cord	1		
Abruptio placentae	1		
<i>Low Forceps: (278)</i>	21, 7.55 %		6, 2.15 %
Maternal toxemia	8	Prematurity	2
Intrauterine asphyxia	4	Maternal toxemia	2
Prolapsed cord	4	Intracranial hemorrhage	1
Macerated	4	Congenital atelectasis	1
Abruptio placentae	1		
<i>Total Results to Child</i>			
Stillborn	71	12.45 %	
Dying in two weeks	30	5.26 %	
Total Infant Mortality	101	17.71 %	

A careful study of the infant mortality reveals a number of causes of death for both stillbirths and infants dying in the first two weeks of life, which are not attributable to the forceps operation. Among the causes of stillbirth in the high forceps group only the 7 cases of intracranial hemorrhage and the 5 cases of intrauterine asphyxia should be attributed to the operation, giving us a corrected stillbirth mortality figure for high forceps of 19.04 per cent. } Of the children dying in the first two weeks

in the high forceps group the one case of hemorrhagic disease of the newborn cannot be attributed to the operation itself and the corrected figure in this instance is 7.93 per cent.

Similarly, in the mid forceps group only the 16 cases of intrauterine asphyxia and 4 instances of intracranial hemorrhage are assignable to the mid forceps operation, giving us a corrected stillbirth mortality figure of 8.7 per cent. Of the infants dying within the first two weeks in this group, the 5 infants dying of prematurity and one of congenital atelectasis may be eliminated as being caused by the forceps operation with a corrected mortality figure of 5.2 per cent.

Similarly, in the low forceps group one may consider only the 4 cases of intrauterine asphyxia and the one case of intracranial hemorrhage as being attributable to the operation, giving a stillbirth mortality figure for this group of 1.43 per cent and for those children dying within the first two weeks of life a corrected figure of 0.359 per cent.

Summarizing this attempt to arrive at a figure representing a corrected infant mortality, we find that the stillbirth rate for high, mid, and low forceps combined is 5.96 per cent. The rate for infants dying within the first two weeks of life for the three groups is 3.15 per cent. These figures compare with the uncorrected mortality figures of 12.45 per cent and 5.26 per cent respectively. The total corrected infant mortality including both stillborn infants and those dying within the first two weeks of life is 9.4 per cent, as compared to 17.71 per cent, the total uncorrected infant mortality is given in Table II.

TABLE III. MISCELLANEOUS

Private	204	36.40%
Service	362	63.96%
White	341	60.24%
Black	225	39.75%
Primipara	419	74.02%
Multipara	147	25.97%
16 years or less	61	10.77%
17 to 25 years	306	54.06%
26 to 35 years	164	28.97%
36 to 50 years	35	6.18%
EPISIOTOMY	FIRST DEGREE TEAR	
263 46.46%	61 10.77%	SECOND DEGREE TEAR
		152 26.85%
		THIRD DEGREE TEAR
		9 1.59%
		(Six of these were occipitoposterior)
CONTRACTED PELVIS (48)	INFANT MORTALITY	
High forceps	7	5 71.42%
Mid forceps	27	9 33.33%
Low forceps	14	3 21.42%

The entire series of cases were classified according to pelvic measurements, and there were found 48 cases of contracted pelvises with external conjugates of 18 cm. or less. It is only fair to state that practically all

of these occurred before the day of the popularity of laparotrachelotomy which has only been in the past few years and today very few of these cases would be subjected to delivery with forceps. The figures on this group of cases are most interesting. There were 7 patients delivered by high forceps with an infant mortality of 71.42 per cent; 27 patients of mid forceps with a mortality of 33.33 per cent; and 14 patients of low forceps with a mortality of 21.42 per cent. The latter group were delivered after a prolonged labor had done its damage to the fetus. It is quite likely that practically all of these 48 cases would be eliminated from this report if the deliveries occurred today rather than a number of years previously.

I have just a word to add in conclusion. From the figures which I have presented, one can, with assurance, draw the conclusion that at best the obstetric forceps is a dangerous instrument which should be used only upon suitable indications and then only by one skilled in its application. There is no place in obstetrics for the so-called "convenience" forceps. Figures on both the immediate and late injuries to the child show beyond a doubt that the higher the station of the fetal head at the time of delivery, the more damage is done. ✓ From 1919 to 1929 1,147 forceps deliveries occurred at the Bonn Woman's Clinic according to H. Krukenberg. The percentage of incidence was 6.2 per cent. Of the live children 72.7 were traced. Fifty-four high forceps revealed 1.9 per cent late injuries; 144 mid forceps revealed 1.4 per cent late injuries; and 739 low forceps revealed 0.13 per cent late injuries. | I apologize for quoting so many statistics but the group of cases traced by Krukenberg is so far superior to any other that I have found in the literature, that I feel the figures are worth mentioning.

F. C. Irving reports 13,849 babies born at the Boston Lying-In Hospital from 1920 to 1929.

Clinically, 99 cases of intracranial hemorrhage were diagnosed or one in every 140 births. From 1909 to 1929, 182 autopsies were performed in which the head was examined. Of these 73 or 40 per cent showed intracranial hemorrhage as the cause of death.

Holland, Spencer, Schott, Archibald, Warwick, Crothers, and others state that intracranial hemorrhage is the most common cause of stillbirth or death within the first few days.

#### SUMMARY

Realizing the high maternal and fetal mortality and morbidity incident to the promiscuous use of the obstetric forceps, I can only plead for less interference in the normal process of labor and the reservation of instrumental delivery for those cases presenting an absolute indication.

## A PRELIMINARY REPORT ON THE USE OF BARBITURATES WITH ETHER BY RECTUM\*

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*(From the Philadelphia Lying-In Maternity Department of the  
Pennsylvania Hospital)*

ONE of the major problems which has always confronted the obstetrician has been the relief of pain during the first and second stages of labor. Many procedures have been enthusiastically endorsed by various men during the past few decades only to be discarded entirely or modified in some manner because of their harmful effect on the mother and child, or because their analgesic power when tried on a large series of cases has been found wanting. The relief of pain in any illness has been one of the chief functions of the practitioner of medicine, and ever since the advent of twilight sleep for the relief of the pain of childbirth, has been one of the important topics of conversation among the laity, and the subject of much literary effort on the part of writers for sundry journals of both good and bad repute.

It is not the purpose of this very short paper to review the many methods that we have used for the relief of pain during labor. During the past year we have had presented a paper on the use of sodium amytal, in which are reviewed the other methods in vogue. I believe that we have no method which in every case gives complete relief from the pains of childbirth. It is therefore important that we continue to investigate all methods suggested.

The most used medication has been morphine and scopolamine in various doses. Following the suggestion of Gwathmey, many of us have used morphine with magnesium sulphate hypodermatically, followed by the instillation into the rectum of ether in olive oil. Some men have found this to be exceedingly satisfactory in their hands, reporting good results in as high as 90 per cent of cases. I do not disagree with these authorities, but must confess that in my own hands it has not been so satisfactory, although we have in selected cases continued its use. The barbituric acid preparations have grown increasingly in popularity as sedatives in the past few years and it remained for Axelrod of Cleveland to suggest the combination of the barbiturates with ether by rectum as an analgesic in labor. This seemed to be a rational outcome of our experience with the Gwathmey technic and the use of sodium amytal both by mouth and intravenously. Axelrod reports a large series with exceptionally good results, so that it was thought advisable on the Vaux Service at the Lying-In Hospital, to try this method for the relief of the pain of childbirth.

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\*Read at meeting of the Obstetrical Society of Philadelphia, March 3, 1932.

The preparation used contains ethyl (one methyl-butyl) barbituric acid, 8 grains; neonal, 5 grains; quinin alkaloid, 20 grains; ether, 2½ ounces; and mineral oil 1½ ounces. The dose is given according to the body weight of the individual, the preparation coming in four ounce containers. The entire four ounces is given to the patient weighing more than 130 pounds; if the weight is less than 130 pounds, the dosage is given accordingly. There are no preliminary hypodermics of morphine or magnesium sulphate.

The contraindications to its use are upper respiratory infections, toxemia, diabetes, nephritis, and auditory disturbances.

The proper time for giving the injection is when the labor is definitely established, with good contractions occurring at least every five minutes, and the cervix beginning to dilate. It is not necessary for the dilatation of the cervix to be advanced to the extent it is advisable in using the Gwathmey technic, as we have had no case, even when given with one finger dilatation, that the labor has stopped.

The method of injection is by a small rectal tube with glass funnel. A small amount of mineral oil is allowed to run in first. The medication is then given followed by another small quantity of either mineral oil or olive oil. The usual precautions as in giving any rectal instillation are carried out. The external parts are thoroughly lubricated. The instillation is given very slowly. The patient is cautioned not to bear down, and pressure is made over the rectum when a contraction occurs. It should take approximately fifteen minutes to give the entire amount. The patient is still kept on her side and pressure made over the rectum for at least a half hour after the injection is given. We have all found in the use of any medication of this kind by rectum, that a great deal depends on the person giving it understanding what should be done, and therefore, in our work at the Lying-In Hospital, only two persons have given these instillations, namely, the day and night anesthetist. We believe rectal analgesics of any kind will have a large percentage of failures if allowed to be given by any nurse who happens to be on duty at the time and who has never had any experience with this method of medication.

Further precaution should be made after giving this medication by not leaving the patient alone at any time after it takes effect. We not only have insisted on having a nurse with the patient at all times, but have constructed a bed similar to a baby's crib, with latticed sides so that if the patient becomes restless, there is no danger of her falling out of bed.

Furthermore, these patients have to be watched more carefully because we have found in several instances the labor has progressed very rapidly, and the patient might deliver herself without being properly prepared.

Although this preparation has been used in more cases than are reported in this series, the first 50 cases only are included in this report as final conclusions have not been drawn, and will not be until a larger series have been given.

This preliminary report is now made to call your attention to this method as it seems to be worth while using.

*Parity.*—In this group of 50 patients, 39 were primiparae and 11 multiparae. These were not selected cases particularly, in order to give this medication to primiparous individuals, but just so happened that the majority admitted on the Service were having their first child. We have found however, in our very limited experience, that the primiparous individual seems to retain the analgesic better and seems to get more relaxation than the multipara. This is probably due to the fact that the pains in the primiparae are not as active and there is less tendency for the membranes to



be bulging through the cervical canal. Furthermore, the sphincteric control of the rectum is better in a woman who has never had a child.

*Time of Giving Analgesia.*—Thirty-eight patients were given the rectal instillation when the cervix was partially effaced and 2 fingers dilated; 7 patients were given it when the cervix was completely effaced and 3 fingers dilated, and 5 patients were given the rectal injection when only 1 finger dilated. As no case ceased to have contractions after the injection, we have continued to give it earlier than we did at first, and there has been no case in this series where labor was definitely established where the contractions of the uterus ceased after it was administered. I believe that this is one of the favorable points in the use of this method, in that it can be given earlier than most sedatives can be used.

*Type of Delivery.*—Forty-one cases were delivered by low forceps; 2 were delivered by decomposition of the breech, and 7 delivered themselves spontaneously. All the cases that were delivered by forceps or breech extraction had ether inhalation to complete the second stage. We have for a number of years delivered most of our primiparae by low forceps under general anesthesia, and we have also delivered our breech cases by decomposing them after the cervix is dilated. Some of these patients delivered by low instruments would have unquestionably delivered themselves if allowed to go on, but we have found that even though the patient had been given this rectal preparation, there was no contraindication to giving a small amount of ether by inhalation in order to keep the patient completely quiet during the delivery. We have found that the breech cases, when this analgesia has been given, are not conscious enough to cooperate in order to deliver themselves spontaneously, and therefore we have continued our usual routine method of delivery. The patients who were delivered spontaneously had no further anesthesia and none of them remember any pain at the time of delivery.

*Results.*—All mothers made uneventful recoveries. One or two complained of some burning about the rectum for a day or two after delivery, and one patient was reported as being incontinent for forty-eight hours. All children were born alive; cried immediately after delivery, and seemed to have suffered no harmful effect from either the rectal instillation or the addition of inhalation anesthesia for forceps delivery. Four patients bled a trifle more than normal, although not enough to warrant packing of the uterus or to call the bleeding a definite postpartum hemorrhage.

*Action of Analgesia.*—It was definitely stated in 42 of these 50 cases that good analgesia had been produced. In other words, in order for us to consider that we had a good result from the injection, patients were quiet, did not complain of pain and did not remember after delivery, what had taken place. When I say that patients were quiet, I mean they were not throwing themselves about the bed or noisy. The usual action was for the patient to move when the uterus would contract, but immediately doze off into deep sleep when the contraction ceased. Even when the head was on the pelvic floor, there would be no unusual action upon the part of any one of these patients, but there were only a few of these 42 who were awake enough to cooperate in bearing down at the end of the second stage. Three patients were reported as having fair results. By fair results we felt that they had some relief from pain but were not relaxed enough to be unconscious of their surroundings, and knew at all times what was going on. One patient became exceedingly irrational and noisy and had to be restrained in bed with a great deal of difficulty. This was a primipara with a long drawn out labor and continued to be irrational until after delivery. Three other patients got no result from the analgesia because they expelled the injections within a half hour after it was given. What happens in these cases is that the injection is retained for fifteen minutes, when it usually becomes effectual. Within a half hour it was expelled without the patient knowing what was happening and within twenty minutes later these patients were perfectly conscious and continued to be so during the rest of their labor. These all occurred in multiparae.

One patient retained the analgesia but got no relief whatever from her pain. She was at no time relieved of pain and remembered everything that happened from the beginning of labor.

*Duration of Analgesia.*—The shortest time after the injection was given before delivery was forty-two minutes, and the longest time eleven hours and fifty minutes. Most of the cases in which we report good results were really not awake for several hours after their return to the Ward, and one patient was aroused with difficulty for a period of eighteen hours.

#### SUMMARY

1. We do not feel that our conclusions can be final at the present time, but the results have been satisfactory enough to warrant the continued use of these drugs for a further time.

2. This method of sedation can be given earlier in the course of labor than most methods in vogue up to the present time.

3. Primiparous patients seem to respond more definitely than do multiparous.

4. If one uses this procedure, he should be prepared to deliver the patient with outlet forceps at the termination of the second stage of labor.

5. There is no contraindication to giving inhalation anesthesia to complete the delivery.

6. There has been no harmful effect upon the mother or the child.

7. These patients should be watched carefully at all times following the injection.

8. The injection should be given by a person who is particularly trained in the administration of rectal medication.

9. There was no evidence of the child suffering from either the injection of the drugs or the small amount of inhalation anesthesia given to the mother at the end of the second stage.

10. Relaxation of the pelvic muscles seem to be better than under ordinary circumstances.

11. There is a tendency, we believe, for slightly more bleeding than normal, but this has not been definitely proved.

12. Protection of the buttocks and the perineum, particularly as small amounts of material is expelled, should be carefully done.

13. Patients given this instillation can not be depended upon to cooperate during the second stage of labor because if not entirely unconscious, are mentally confused to the point of being irrational.

14. The contraindications as listed above should be particularly stressed, and especially toxemia where the amount of liver damage is not definitely known, as the therapeutists tell us that the barbituric acid preparations are eliminated principally through this organ.

15. In our limited experience this method of analgesia has proved satisfactory enough and not fraught with any danger, so that we will continue its use until a larger series has been collected.

# TEMPORARY STERILIZATION BY THE INJECTION OF HUMAN SPERMATOZOA. A PRELIMINARY REPORT

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THE possibility of immunization of females by injection of spermatozoa is not new. It is only recently, however, that experimental work has been directed with the view of determining the practical application of such an immunization on animals and human beings.\*

\* \* \* \*

From the extensive literature, although somewhat contradictory, we may draw the following conclusions:

1. Immunization is possible by injection of spermatozoa.
2. This immunization is specific for tissue and species, noting exceptions, ram and bull.
3. Large quantities of antigen are necessary for active immunization.
4. The immunization is apparently harmless and varies with the amount injected.

On this basis we began in April, 1929, the injection of human females with male spermatozoa. Our first case is then over two years old. The technic employed has been the same in all cases. Twenty women have been injected.

We are not attempting to draw any but the most general conclusions. Some of our cases are too recent to judge. We know there are a number of things to be worked out, but certain conclusions naturally follow from these. The technic has been as follows: Intercourse per condom. The specimen was tied and brought to the office as soon as possible. One cubic centimeter of hexylresorcinol was added. The entire amount was drawn into a syringe and injected into the buttocks. No semen was used with a count of less than 80,000,000 per cubic centimeter; three injections given seven days apart. The amounts of semen varied from 2 to 5 c.c. It is, of course, impossible to standardize a procedure with varying amounts. The exact amount necessary and number of injections will have to be determined by further work. Three cubic centimeters was the average amount, so that it may be stated that at least 9 c.c. were injected in every case, except one. The largest amount injected was 14 c.c. of semen.

One week following the last injection the serum was tested and tests were run every three months. The injections produced no constitutional symptoms. Local pain of moderate degree was present for about twenty-

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\*For lack of space the author's extended review of the literature is omitted from the JOURNAL, but will be available in his reprints.

four hours after the first injection. There is markedly less after the second injection and after the third injection there is practically no pain.

The immunized serum was examined as follows: Three slides were prepared. One with human spermatozoa, one with spermatozoa to which nonimmunized blood serum was added, and one with human spermatozoa to which immunized serum was added. Slides were examined every fifteen minutes. In no case was there noted any delay in motility with the normal serum. The spermatozoa in these slides lived as long as in those to which no serum had been added. Under the conditions in our laboratory where spermatozoa were examined, sperms lived more than six hours if they had not been chilled. They were not examined after that time. Cervical secretions were also tested against sperms in every case.

CASE 1.—Aged twenty-five, 2 pregnancies.

Injected April 7, 14, 21, 1929, total 9 c.c.

- 1 wk. Sperms dead 30 min.
- 3 mo. Sperms dead 30 min.
- 6 mo. Sperms dead 45 min.      All controls alive 6 hr.
- 9 mo. Sperms dead 2½ hr.
- 12 mo. Sperms dead 4 hr.

Cervical secretions negative at every examination.

Reinjected May 2, 9, 16, 1930, total 9.5 c.c.

- 1 wk. Sperms dead 30 min.
- 3 mo. Sperms dead 30 min.
- 6 mo. Sperms dead 30 min.      All controls alive 6 hr.
- 9 mo. Sperms dead 45 min.
- 12 mo. Sperms dead 45 min.
- 15 mo. Sperms dead 45 min.      (Aug. 1931)

Cervical secretions negative throughout.

CASE 2.—Aged thirty-nine, 4 pregnancies.

Injected June 2, 9, 16, 1929, total 11 c.c.

- 1 wk. Sperms dead 45 min.
- 3 mo. Sperms dead 45 min.
- 6 mo. Sperms dead 75 min.      All controls alive 6 hr.
- 9 mo. Sperms dead 2 hr.
- 12 mo. Sperms alive 6 hr.

Reinjected July 3, 10, 17, 1930, total 11.5 c.c.

- 1 wk. Sperms dead 30 min.
- 3 mo. Sperms dead 30 min.
- 6 mo. Sperms dead 60 min.      All controls alive 6 hr.
- 9 mo. Sperms dead 60 min.
- 12 mo. Sperms dead 90 min.

Cervical secretions negative throughout.

CASE 3.—Aged twenty-two, 1 pregnancy.

Injected December 7, 14, 21, 1929, total 9.5 c.c.

- 1 wk. Sperms dead 75 min.
- 3 mo. Sperms dead 75 min.

6 mo. Sperms dead 75 min.      All controls alive 6 hr.  
 9 mo. Sperms dead 2 hr.  
 12 mo. Sperms dead 2 hr.  
 15 mo. Sperms alive 6 hr.  
 Cervical secretions killed sperms instantly on two examinations, 3 mo. and 9 mo. All other examinations with cervical secretions negative.

Reinjected June, 1931, total 12 c.c.

1 wk. Sperms dead 15 min.

Cervical secretions negative.

CASE 4.—Aged thirty-six, 5 pregnancies.

Injected January 4, 11, 18, 1930, total 11.5 c.c.

1 wk. Sperms dead 75 min.

3 mo. Sperms dead 75 min.      All controls alive 6 hr.

6 mo. Sperms dead 3 hr.

9 mo. Sperms alive 6 hr.

Cervical secretions negative. Patient lost track of.

CASE 5.—Aged thirty-three, 3 pregnancies.

Injected March 10, 17, 24, 1930, total 14 c.c.

1 wk. Sperms dead 30 min.

3 mo. Sperms dead 30 min.

6 mo. Sperms dead 30 min.      All controls alive 6 hr.

9 mo. Sperms dead 60 min.

12 mo. Sperms dead 90 min.

15 mo. Sperms dead 2 hr.

Cervical secretions negative.

CASE 6.—Aged thirty-seven, 3 pregnancies.

Injected March 15, 22, 29, 1930, total 12 c.c.

1 wk. Sperms dead 15 min.

3 mo. Sperms dead 15 min.

6 mo. Sperms dead 15 min.      All controls alive 6 hr.

9 mo. Sperms dead 30 min.

12 mo. Sperms dead 30 min.

15 mo. Sperms dead 90 min.

Cervical secretions negative.

CASE 7.—Aged thirty-two, 4 pregnancies.

Injected May 2, 9, 16, 1930, total 13.5 c.c.

1 wk. Sperms dead 30 min.

3 mo. Sperms dead 45 min.

6 mo. Sperms dead 45 min.      All controls alive 6 hr.

9 mo. Sperms dead 2 hr.

12 mo. Sperms alive 6 hr.

Became pregnant June, 1931, cervical secretions negative.

CASE 8.—Aged twenty-nine, 3 pregnancies.

Injected May 6, 13, 20, 1930, total 11.5 c.c.

1 wk. Sperms dead 15 min.

3 mo. Sperms dead 15 min.

6 mo. Sperms dead 45 min.      All controls alive 6 hr.

9 mo. Sperms dead 45 min.

12 mo. Sperms dead 90 min.

15 mo. Sperms dead 4 hr.

Cervical secretions positive at 6 mo. examination only.

## CASE 9.—Aged thirty-six, 4 pregnancies.

Injected December 2, 9, 16, 1930, total 9.5 c.c.

1 wk. Sperms dead 45 min.

3 mo. Sperms dead 60 min. All controls alive 6 hr.

6 mo. Sperms dead 90 min.

9 mo. Sperms dead 3 hr.

Cervical secretions negative.

## CASE 10.—Aged twenty-four, 1 pregnancy.

Injected January 4, 11, 18, 1931, total 11 c.c.

1 wk. Sperms dead 15 min.

3 mo. Sperms dead 15 min. All controls alive 6 hr.

6 mo. Sperms dead 15 min.

9 mo. Sperms dead 60 min.

Cervical secretions positive. (Killed sperms 5 min. at first examination and 9 mo. examination.) Negative at other examinations.

## CASE 11.—Aged twenty-three, 1 pregnancy.

Injected February 5, 12, 19, 1931, total 12.5 c.c.

1 wk. Sperms dead 15 min.

3 mo. Sperms dead 15 min. All controls alive 6 hr.

6 mo. Sperms dead 60 min.

Cervical secretion positive all examinations. Killed sperms on contact.

## CASE 12.—Aged thirty, 3 pregnancies.

Injected February 9, 16, 23, 1931, total 10 c.c.

1 wk. Sperms dead 30 min.

3 mo. Sperms dead 45 min. All controls alive 6 hr.

6 mo. Sperms dead 90 min.

Cervical secretions negative.

## CASE 13.—Aged twenty-seven, 2 pregnancies.

Injected March 6, 13, 20, 1931, total 9.5 c.c.

1 wk. Sperms dead 30 min.

3 mo. Sperms dead 60 min. All controls alive 6 hr.

6 mo. Sperms dead 60 min.

Cervical secretions negative.

## CASE 14.—Aged thirty, 1 pregnancy.

Injected April 16, 23, 30, 1931, total 11 c.c.

1 wk. Sperms dead 75 min. All controls alive 6 hr.

3 mo. Sperms dead 2 hr.

Cervical secretions negative.

## CASE 15.—Aged twenty-eight, 3 pregnancies.

Injected April 23, 30, and May 9, total 11 c.c.

1 wk. Sperms dead 15 min. All controls alive 6 hr.

3 mo. Sperms dead 45 min.

Cervical secretions negative.

## CASE 16.—Aged twenty-six, 1 pregnancy.

Injected May 8, 15, 21, 1931, total 10.5 c.c.

1 wk. Sperms dead 75 min. All controls alive 6 hr.

3 mo. Sperms dead 75 min.

Cervical secretions negative.

CASE 17.—Aged twenty-six, 4 pregnancies.

Injected June 11, 18, 25, 1931, total 14 c.c.

1 wk. Sperms dead 5 min. All controls alive 6 hr.

3 mo. Sperms dead 15 min.

Cervical secretions negative.

CASE 18.—Aged twenty-two, 2 pregnancies.

Injected June 14, 20, 27, and July 3, 1931, total 5 c.c.

1 wk. Sperms alive 6 hr. (4 injections)

No results. Amount probably too small.

CASE 19.—Aged twenty-two, 1 pregnancy.

Injected June 12, 19, 26, 1931, total 11 c.c.

1 wk. Sperms dead 15 min. All controls alive 6 hr.

3 mo. Sperms dead 30 min.

Cervical secretions positive (15 min.) both examinations.

CASE 20.—Aged twenty-eight, 4 pregnancies.

Injected August 22, 29, September 4, 1931, total 14 c.c.

1 wk. Sperms dead 15 min. Control alive 6 hr.

Cervical secretions negative.

It will be noted from the above cases that a definite immunity was established in all cases except one (Case 18). It is probable that this patient did not receive enough semen. The total amount injected in this case was 5 c.c. for four injections. The next smallest amount injected was 9.5 c.c. These patients showed an immunity for a number of months.

None of the above cases showed any constitutional symptoms. There were no local symptoms except soreness for twenty-four hours. One patient, not listed, developed a small abscess. As the injections were not finished, this case is not recorded. Smears in this case failed to reveal an organism and abscess healed in a few days.

No patient became pregnant while her blood showed a definite toxic principle for spermatozoa. One patient (Case 7) became pregnant one year after injection. Reinjection seems to prolong the immunity. Just how long the immunity remains after reinjection is as yet impossible to state. We have not encountered any case in which the immunity does not disappear. The question of permanent sterility does not seem likely, at least after one series of injections.

We have not been able to demonstrate any individual specificity. Repeated examinations of immunized sera against spermatozoa from other males have shown no differences.

There has been no change in course, duration or character of menses in any case. If the work of Megliavacca<sup>32</sup> is correct such a change might be expected, but did not occur in our cases.

The varying results with cervical secretions were puzzling. Spermatotoxic properties were demonstrated at times and not at others. Close questioning disclosed the fact that where cervical secretion was positive, the patient had had an orgasm. This result is being watched further.

It is possible that cervical secretion during intercourse is spermatotoxic, while the normal secretion is not.

Each individual case requires such cooperation that the method is not practical at the present time on a large scale. If it were possible to use spermatozoa of some other animal, the work would be much simplified. We are at present attempting this on animals. It may be possible to destroy the species specific properties of some animal spermatozoa.

A number of questions must be answered concerning this work. Principally among these are: first, possibility of permanent sterility; second, whether ovarian changes occur; third, whether there is any effect on future generations. We are now carrying on work in an attempt to answer these questions.

#### CONCLUSIONS

1. Immunization of women with human spermatozoa is possible.
2. The immunization lasts about one year.
3. Revaccination at end of year prolongs the immunity for at least another year.
4. The period of immunity and degree of immunity can be determined by the blood.
5. Spermatotoxic properties of cervical secretions are not constant.
6. The injections are harmless to the patient.

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# THE SLOWING OF THE FETAL HEART AND ITS RELATION TO THE FETAL-PLACENTAL CIRCULATION\*

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THE importance of auscultating the fetal heart during labor is well recognized. When the rate drops below 80 during a pain and does not return to above 100 in the interval, it is a sign of imminent danger to the child. While we have learned from clinical experience its significance, the mechanism that causes this slowing of the fetal heart is rather obscure.

A number of theories have been offered at various times to account for this occurrence. Two of them are generally accepted as explaining this condition.

Schultze, in 1871, claimed that during a strong contraction the blood supply to the uterus is interfered with, the placenta compressed, and its circulation disturbed. Proper oxygenation of the fetal blood does not occur and an excess of  $\text{CO}_2$  accumulates, which stimulates the vagus and thereby slows the fetal heart.

The other theory is that strong pressure on the fetal head increases intracranial pressure and thereby causes the slowing.

The assumption that a strong uterine contraction interferes with the uterine circulation is not tenable. During pregnancy there is an increase of fat and muscle tissue in the uterus, which serves to protect the blood vessels from undue pressure. This is evident from the fact that after delivery, when the uterus is empty, it is reduced in size and remains contracted, yet there is no shutting off of the blood supply in the uterus sufficiently to interfere with its circulation. The contraction of the uterus and placenta no matter how severe, would not hinder the exchange of gases between the uterus and placenta, as long as the placenta remains attached.

Assuming that  $\text{CO}_2$  is the factor which slows the fetal heart, we must consider the duration of time that the placental circulation would have to be obstructed in order to have sufficient  $\text{CO}_2$  accumulate to act as a stimulant. A moderate slowing of the fetal heart occurs promptly with every contraction of the uterus; and the same mechanism which causes this normal slowing also produces the pathologic slowing. The normal slowing occurs so promptly with each pain, that there cannot be any accumulation of  $\text{CO}_2$  in that instant. Even with a severe contraction sufficient time does not elapse to make any appreciable difference in the amount of  $\text{CO}_2$ . We know that in breech deliveries when the cord is completely compressed by the aftercoming head, it takes a considerable time before sufficient  $\text{CO}_2$  accumulates to stimulate the respiratory center. Therefore it is unlikely that every time there is a contraction,

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whether ordinary or severe, there is an increase of  $\text{CO}_2$  in sufficient quantity to disturb the fetus.

The entire theory rests on the assumption that  $\text{CO}_2$  acts as a vagus stimulant. There is no evidence however that  $\text{CO}_2$  has any direct influence on the vagus. Consequently all the explanations of how  $\text{CO}_2$  is produced during a contraction are irrelevant. Carbon dioxide is definitely a respiratory stimulant. Whenever there is an increase of  $\text{CO}_2$ , the respiratory center is stimulated. When the baby is born, the separation of the placenta causes the accumulation of  $\text{CO}_2$  which starts respiration. Any intrauterine increase of  $\text{CO}_2$  would cause the baby to breathe, rather than a slowing of the fetal heart.

It is therefore evident that the theory of an increase of  $\text{CO}_2$  as a cause of slowing of the fetal heart should be discovered.

The objections to the theory that pressure on the fetal head produces slowing of the fetal heart are well stated by Seitz as follows: The pressure on the head during a pain is no more than the pressure on the rest of the fetus. The blood supply to the brain is abundant and is therefore not deficient during a compression. In cases of cerebral hemorrhage, meningitis, and other conditions where we know that the intracranial pressure is increased, the heart does not slow down to such an extent as it does in the fetus during a labor pain. He also claims that compression of the head with forceps does not slow the fetal heart, but accepts the theory of increased  $\text{CO}_2$  as producing the slowing.

Baumm, Sachs, and Seitz while they accept one or both theories, quote numerous cases where the slowing of the fetal heart or the death of the fetus could not be accounted for by either of the two explanations.

The mechanism which causes the fetal heart to slow down, appears to me, to be produced as follows: We know that the same blood circulates in fetus and placenta. The total volume is about 400 c.c. and is maintained at a definite pressure in both.

When a uterine contraction occurs, the placenta is compressed and a variable amount of blood from the placenta is forced out of it into the fetus. This increases the quantity of blood in the fetus, raises the pressure in the fetal circulation and thereby causes a slowing of the fetal heart. That an increase of blood volume and blood pressure produces a slowing of the heart is a known physiologic fact. It is in accordance with "Marey's law," which states that the pulse rate varies inversely as the blood pressure. This should also apply to the fetal circulation. When the uterine contraction subsides and the pressure on the placenta is relieved the excess blood flows back into the placenta, the tension is reduced and the fetal heart returns to its normal rate.

When, however, the uterine contractions become very strong, there is an exaggeration of this process. More blood is forced into the fetus than with a normal contraction, there is therefore a greater slowing of the heart, and as the contraction lasts longer, the slowing persists for a greater time. Even when the pain is over the uterus does not relax en-

tirely, the excess blood does not return altogether to the placenta, so that the fetal heart does not return to its normal rate. When however the uterus does relax and the tension is relieved; the heart returns to its usual pace and the condition is normal again. But when the strong contractions persist, and before the heart has had a chance to recover its normal rate another contraction occurs, and more blood is forced into the fetus, the tension is further raised, the heart is still further slowed, it becomes distended, and if this continues the heart dilates and then stops entirely. It is, as if the fetus continued to be transfused with an excess of blood. To use a term applicable in this motor age, we would say that the heart stalls from being overloaded.

When the membranes have ruptured the uterus is reduced in size and the placenta is compressed. The placenta therefore cannot hold as much blood as before and the fetus must carry a greater share. With each pain the placenta is further compressed, and to a greater extent than when the membranes are intact, so that the fetal heart is more apt to be slowed after the membranes had ruptured.

When ether or chloroform is administered to the woman the uterus relaxes, the pressure on the placenta is relieved, the tension in the placenta and fetus is reduced, and the fetal heart returns to normal. If the baby is delivered the pressure is removed and the child is saved providing the fetal heart has not been overstrained nor has any hemorrhage occurred in the fetus in the meantime, as a result of this increased tension.

The increased blood volume which slows the fetal heart also causes a congestion of all fetal organs. The splanchnic area gets a large part of it. This produces a congestion of the bowels which sets up peristalsis and causes the escape of meconium. It is therefore evident why the passage of meconium and the slowing of the fetal heart are concomitant events, since they are both produced by the same force. When meconium is noticed, it is evidence that there had occurred an overloading of the fetal circulation which is apt to be repeated. The heart sounds under the circumstances need extra watching.

This increased tension in the fetal circulation, also may cause ruptures of the blood vessels in the fetus, particularly those in the brain. The tension in the blood vessels when the uterus contracts is enormous, as can be demonstrated when the cord is cut without tying. This will explain how the fetus sustains a cerebral hemorrhage in a spontaneous delivery, without any undue pressure on the head from the outside. The other hemorrhagic lesions of the fetus which are attributed to asphyxia, are produced by the increased volume of blood and increased pressure during a severe contraction.

T. R. Ford and others have produced asphyxia in experimental animals, and have shown that hemorrhages do not result from it, regardless of the degree of asphyxia. Cerebral hemorrhage in the newborn can cause asphyxia, but asphyxia does not produce hemorrhages.

In prolapse of the cord, when the cord is compressed completely, and the circulation is entirely shut off, the respiratory center is stimulated by the accumulation of  $\text{CO}_2$ , and as respiration is impossible the fetus suffocates. But usually the pressure on the cord is not complete, and a different process then takes place. The force of a uterine contraction increases the tension in the cord and enables it to withstand the pressure; so that blood is forced into the fetus. The blood cannot return to the placenta as the systole of the fetal heart is unable to overcome the obstruction. The fetal circulation therefore becomes overloaded, the heart rate becomes slower and slower, and if the condition is not relieved the heart dilates and stops.

The question arises why in certain cases a serious slowing of the fetal heart occurs, while in other cases with apparently equally strong pains, there is no effect on the rate. It must depend on several factors; first, the location of the placenta; second, the size of the placenta; third, the volume of blood in the placenta and fetus. When the placenta is located at or near the fundus in the most contractile part of the uterus, it will be compressed to a greater extent than when it is located in the lower portion. Hence more blood will be forced out of it during a pain, and a slowing of the heart will occur. If the placenta is disproportionately large it will hold a larger quantity of blood, and a greater amount of blood will be forced out of it during a contraction than from a smaller placenta, and an overloading of the fetal heart will occur. Or there may be a plethoric condition of the fetus and placenta, the volume of blood in both being large, in which case the fetus is unable to stand the extra supply which it gets from the placenta during a contraction. These conditions we cannot fortell nor can we change them. All we can do is to be on a constant lookout for a slowing of the fetal heart.

The last supposition suggests an explanation for those cases where the fetus dies at the very onset of labor. The fetus continues to develop normally during pregnancy, but with the onset of labor pains the fetal heart stops. This condition frequently is repeated in several pregnancies in the same patient. At autopsy no pathologic lesions are found. A prolapsed or twisted cord is assumed to be the cause of these deaths but usually none is found to account for it. What happens is similar to the condition mentioned above. Due to some factor in the development of the fetus an excess of blood is produced, which is the maximum the fetus and placenta can hold. At the onset of labor with the first contraction, the heart is overloaded and the fetus succumbs. In a patient that has had this unfortunate occurrence repeated, elective cesarean section saves these babies by preventing the overloading of the fetal heart. These children show no abnormalities after birth to otherwise account for their precarious intrauterine condition.

When the baby is delivered, and the heart beats very slowly, or is hardly perceptible, one method of stimulating the heart is to cut the cord without tying and allowing some blood to escape. This relieves

the overload on the heart. More effectual, is mouth to mouth respiration. By distending the baby's chest, the lungs draw in a quantity of blood which relieves the overload on the heart. At the same time the respiratory system is set in motion, the heart rate increases, and the baby continues to breathe regularly.

The sympathetic nervous system is not fully developed in the fetus, and there is no evidence of the placenta being supplied with these nerves. The question arises, how is the blood pressure in the fetus and placenta maintained? The likely explanation is that the placental and fetal circulation derives its tone from the uterus. It is the tonic state of the uterus, which holds the placenta in place and properly contracted. This contraction maintains the pressure in the placental circulation, which in turn is transmitted to the fetal circulation. Should the uterus, for some reason suddenly relax, pressure in the fetal and placental circulation would drop and the fetus would go into shock. This, I believe, explains how death of the fetus occurs when the mother suffers a sudden nervous shock. A general relaxation takes place in all abdominal viscera of the mother. The uterus loses its tone and relaxes, this removes the tone from the placenta and the vessels dilate. The blood from the fetus flows out of it into the placenta, the blood pressure drops, and the fetus goes into shock and dies.

#### SUMMARY

The accepted theory that the slowing of the fetal heart is produced by an interference with the oxygenation of the fetal blood and consequent increase of  $\text{CO}_2$ , which stimulates the vagus, is erroneous.

Pressure on the fetal head, also, does not explain the slowing of the fetal heart.

The slowing of the fetal heart is produced by the contraction of the uterus compressing the placenta and forcing some blood out of it and into the fetus. This increases the volume and tension in the fetal circulation which causes the heart to slow down. With a severe pain this process is exaggerated and an extreme slowing occurs.

The increased blood volume during a severe contraction also produces a congestion of the bowels, which stimulates peristalsis and causes the escape of meconium at the same time that the slowing of the fetal heart occurs.

The increased volume and tension in the fetal circulation can cause rupture of the fetal blood vessels, with hemorrhages in the brain or other organs. These hemorrhages cause asphyxia, but asphyxia does not produce hemorrhages.

In prolapse of the cord the slowing of the heart is produced by an overloading of the fetal circulation. The blood from the placenta is forced into the fetus, but the blood is unable to return to the placenta due to the compression of the cord.

Death of the fetus at the onset of labor is produced by an overloading

of the fetal heart, in those cases where there is an excess of blood in the fetal-placental circulation.

When the mother suffers a sudden nervous shock, death of the fetus is produced by a relaxation of the uterus and placenta. This causes the blood to flow out of the fetus and into the placenta, thereby producing a fatal anemia in the fetus.

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15 EAST ONE HUNDRED ELEVENTH STREET.

### THE INDICATIONS FOR STERILIZATION\*

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STERILIZATION with its indications is a subject which is constantly being brought to the attention of the busy general practitioner and the obstetrician connected with an active clinic. In spite of this there are very few references to the subject in the Obstetrical Literature, the standard textbooks dismissing the indications with a very few lines, and devoting but little more space to the various methods. DeLee says, in effect, that any disease which is a contraindication to pregnancy is an indication for sterilization, and allows the matter to rest there. A search of independent literature is almost as barren, the most notable exception being Williams' most valuable article in the *Journal of the American Medical Association* in 1928.

The subject is one which is very much to the fore at the present time, and the only way any unanimity of opinion may ever be reached is for everyone to be perfectly frank about his own opinions and his work. In this way there will at least be a basis for argument and something from which those with more limited experience may draw conclusions.

In the past eleven years at the University Hospital, sterilization has been considered necessary or advisable in 55 instances. Since 10 of these were Porro sections, in which infection was the indication in 6 cases, obstructive tumors in 2, and abruptio placentae and cervical carcinoma (really a panhysterectomy) in 1 each; the operation was intentional 45 times. There occurred in the clinic over this same period 20,458 deliveries, giving a sterilization incidence of 1 in 454 deliveries.

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The indications are several and the methods used vary somewhat and our views and results are offered with the hope of stimulating discussion and prompting others to report their experiences also.

## INDICATIONS

*Incidental Group (Porro operations)*

1. Prolonged labor with infection	6
2. Obstructive tumors	2
3. Abruptio placentae	1
4. Carcinoma of cervix (panhysterectomy)	1

*Intentional Group*

1. Cephalopelvic disproportion with repeated sections, 3 or more	17	37.7%
2. Nephritic toxemia with multiparity	7	15.5%
3. Heart conditions complicating pregnancy	6	13.3%
4. Low mentality (repeated pregnancies with mentally defective children)	6	13.3%
5. Epilepsy	3	6.6%
6. Placenta previa and multiparity	2	4.4%
7. Chorea	2	4.4%
8. Tuberculosis, pulmonary	2	4.4%
Total	45	100. %

Of the 10 cases in which the uteri were removed, the 6 done for infection all occurred before the extensive use of laparotrachelotomy, and were they to come under our care today, it is probable that this would be the procedure in most of them. The remaining 4 need no comment other than that it is surprising that we have not found it necessary to remove more uteri for abruptio placentae.

(Our noncorrected maternal mortality for this condition over the period covered by this report is 6.85 per cent.)

Of the 45 cases in the intention group, 17 were done because of cephalopelvic disproportion, all of the patients having had 2 or more cesarean sections prior to the one accompanied by sterilization. It seems unfair to expose the mother of a family of this size to the dangers of further pregnancies and operations.

Next in order of frequency is nephritic toxemia with 7 instances, then heart conditions and low mentality, 6 of each.

The cases of nephritic toxemia were all cases which we had cared for repeatedly in our Clinic and in which evidence of increasing kidney damage had been noted with successive pregnancies. To merely carry a case of this kind through her pregnancy, to deliver her of a premature child, either stillborn, weak or puny, with little chance of surviving, and to discharge her with the warning that she must not become pregnant, is to treat her very inadequately. The present status of the various contraceptives is such that they are of little or no value to the clinic type of patient, and of not much more to anyone. So that if pregnancy is very evidently contraindicated, there is little else to do other than to sterilize.

Of the heart conditions which were deemed sufficiently grave to warrant sterilization, 4 were primiparae, 1 a para ii and 1 a para iii. They had all suffered decompensation at one time or another, and none probably should

have become pregnant at all. Pregnancy having occurred, however, it did not seem that anything was to be gained by interruption, and indeed, all of these women went through their pregnancies remarkably well, requiring very little treatment. Rest was insisted upon, and occasionally digitalis was given. Local anesthesia was used 5 times and avertin once.

The low mentality cases were all seen by consultants of the psychiatric department, they were all multiparae, and all had mentally defective children. The sterilization was not only recommended but urged by the consultants in all of these cases.

There were 3 cases of epilepsy, 2 of them primiparae, and the third a para ii, with one child, a hopeless idiot. Operation in all of these cases was also done only after psychiatric consultation.

The 2 patients with placenta previa who were sterilized were both multiparae (para xi or xii), on whom cesarean section was done because of central placenta previa, and the sterilization was more or less incidental.

One of the cases of pulmonary tuberculosis was a para ii, the first labor nine years before having been terminated by cesarean for maternal exhaustion. She had had one kidney removed two years before this for tuberculosis and after delivery her chest condition became active and she was in a sanatorium for several years, from which she was finally discharged as an arrested case. She was seen early in this pregnancy and was referred to 3 competent internists. Their consensus of opinion was that she was quiescent and that the pregnancy should be allowed to continue. Section and sterilization under local anesthesia were done at term, with very pleasing results for both mother and child. The other was a para viii with a healed tubercular lesion who was sectioned for placenta previa and sterilized at the same time. The 2 cases of chorea also exhibited a very low mentality and were obviously unfit for motherhood.

#### METHODS OF STERILIZATION

Unless there seemed a pathologic indication to do so, none of our cases were sterilized by hysterectomy. In 18 cases the tubes were resected and the ends buried and in 27 Madlener's technic, kinking, crushing and tying of tube, was followed. There was at first considerable criticism of this method by our own clinic members, but it has gradually subsided to a low murmur and with one exception we are now all in accord that it is simple and as safe as any in which a removal of uterus, tubes and ovaries is not resorted to.

In this connection it is interesting to note the change in attitude of one of the outstanding obstetric authorities of our country. In 1926 he stated that it might be used when time was an important element, but that he did not fully trust it. In 1927 he had begun to use it but was not ready to report upon it. In 1929 it was declared to be "almost as positive as tubal excision, if not its equal." In 1930, "one of the surest, easiest, and safest of methods." This method has the added advantage that the tube may later be reunited if desired. It readily lends itself to local anesthe-



sia, and is not complicated by any bleeding at all. We have had no failures from this method and in the literature there are remarkably few (1 in 545 cases, and 2 more without any statement as to the number of cases) so few indeed that when they do occur, an error in technic, as simple as it is, may be suspected. Of the cases sterilized by resection of the tubes, 18 in number, one later became pregnant and returned to us. She was one of the contracted pelvis series, was again sectioned and *resterilized*. The entire group of 55 offered nothing else of interest either in mortality or morbidity.

#### DISCUSSION

What, then, are the indications for sterilization? The list is a long one and many of the indications must, of necessity, be very elastic. The number of children already born, the desire for children, the general condition of the mother in addition to the specific indication, and many other things will all have to be considered before a decision may be reached.

When the question arises in our own clinic, we have been in the habit of referring the patient to the necessary consultants, and then when all of their opinions are at hand the case is brought up for discussion before as many members of the obstetric group as can be present. Everyone feels free to voice his opinion and after a full discussion, the question is decided.

Parenthetically it is interesting to note that since we have been doing more sterilizations, the question of the interruption of pregnancy arises less and less frequently. The case of epilepsy with one child, an idiot, was sent us for interruption. We allowed her to go to term and two years later the psychiatrists reported that the baby was apparently of normal mentality.

The kidney and heart cases have already been discussed, and need no additional comment. In tuberculosis, the internist must be listened to very closely and his advice should bear great weight. In contracted pelvises, if the mother is in otherwise good condition, the procedure need not be considered until the third delivery, or under special conditions, the fourth or fifth. Cesarean section on selected cases, properly prepared and done as an operation of choice should give excellent results in competent hands.

Low mentality has given us the most concern of all the indications we have met. Many of our patients had given indications of being unfit for motherhood, and others were already the mothers of mentally defective children, and would apparently continue to bring such children into the world if nothing were done. Any contraceptive advice is of course useless in these cases, and sterilization is the only means of controlling them. Psychiatric consultation is always requested when a question of mentality arises, and the department has given us most whole-hearted cooperation, as indeed have all the other consultants we have called upon.

Only a few of the more outstanding indications have been considered

here, but I am sure that with other contributions to this subject the list will rapidly grow.

In the preparation of this paper I have carefully reviewed the cases in the series, and with the exception of the Porro sections, the most of which would have laparotrachelotomies today, I found none which in retrospect offered a weaker indication that it did at the time of operation.

If a cesarean section seems too drastic a procedure, it is a perfectly simple matter to allow labor to proceed in the usual manner and to open the abdomen during the puerperium. The sterilization may then be done by any method desired.

MEDICAL ARTS BUILDING.

## REPORT OF A CASE OF RAMIFYING ANGIOMYOMA OF THE UTERUS

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UTERINE neoplasms composed essentially of blood vessels, or presenting blood vessels as conspicuous features, are unusual. Recently Horgan<sup>1</sup> reported a case and reviewed 21 cases previously reported. He separates these into four groups: (1) true cavernous hemangiomas in the wall of the uterus without fibromyomas, (2) hemangiomatous fibromyomas, (3) telangiectatic hemangiomas in the pelvis, and (4) a doubtful case of hemangioma in the cavity. Where recorded, recovery is given as the clinical result in all except one case; in this, death occurred a few days after operation. In addition, angiomyomas uteri have been reported by Mandelstamm,<sup>2</sup> Ehnmark,<sup>3</sup> Erede,<sup>4</sup> Neumann,<sup>5</sup> and Tarlo<sup>6</sup> during the last five years, while during the same period Brodersen<sup>7</sup> reported a case of angioma mucosae uteri. Frank<sup>8</sup> has reported a case of hemangioma of pelvic connective tissue. Still others refer to intra-uterine phlebectasia of angiomatous type<sup>9</sup> and to proliferations of blood vessels and of lymph vessels in myometrium and myomas.<sup>10</sup> A complete review of the literature will not be attempted.

### REPORT OF CASE

*Clinical Data.*—H. M., negro, aged thirty-three, single, was admitted to the surgical service of the Hospital Division of the Medical College of Virginia on August 15, 1930, complaining of pain in the lower right quadrant of the abdomen and in the lumbar region of the back. The onset had been about seven weeks previous to admission. During most of this interval the patient had been in bed. The lower abdominal pains were colic-like in character. Nausea, vomiting, and loss of appetite were associated. There had been a leucorrhea of a yellow color, which lately had disappeared. On two previous occasions there had been attacks similar to the present. The family history was unimportant.

On admission the patient was well nourished, well developed, and did not appear to be acutely ill. Pyorrhea was noted. The heart and lungs were regarded to be normal. The abdomen was not rigid and moved freely with respiration. On palpation tenderness was noted over the entire right side, most marked in the lower right quadrant. No masses could be felt. Tenderness was noted in the right lumbar region. Vaginal examination revealed a dilated soft cervix and gave an impression of fullness on the right side. The body temperature was 98° F., the pulse 80, and respirations 22.

The preoperative clinical diagnosis was chronic salpingitis with chronic appendicitis. Laparotomy was performed by Dr. Webster P. Barnes on August 18 under spinal anesthesia. There was a right indirect inguinal hernia with a piece of omentum adherent to the orifice. The fundus of the uterus had the size of a duck egg.

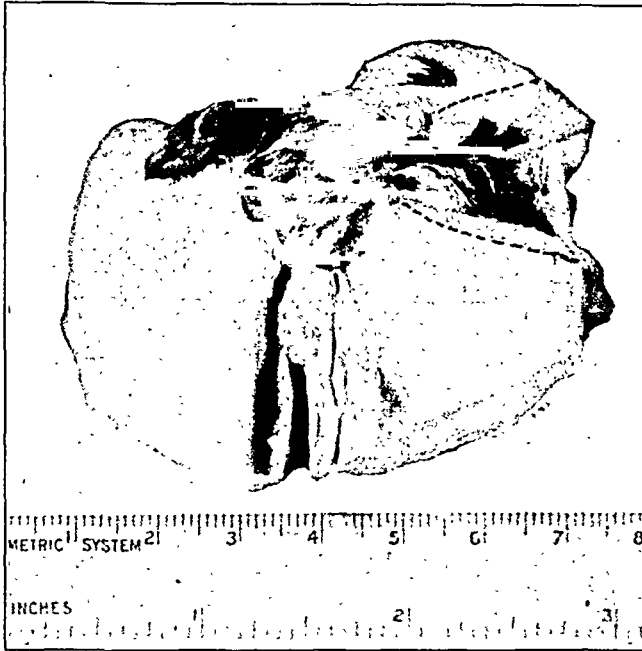


Fig. 1.—The gross specimen with ramifications of the tumor (shaded portion) bulging from cut surfaces of the fundus. The broken lines indicate edges left after removal of a wedge-shaped piece of tissue from the cornu.



Fig. 2.—Cord-like structure of much of the tumor, with the cord shown composed of blood vessel axes having perivascular bundles of smooth muscle cells.

Adhesions bound both fallopian tubes, with numerous serous retention cysts associated with the surface of the right tube. The hernial sac was removed from within. The body of the uterus, both fallopian tubes, right ovary and appendix were removed.

*The Specimen.*—The specimen received consisted of the body of a uterus with both fallopian tubes and right ovary attached, a semitransparent serous retention cyst

3 cm. long, and an appendix. The fallopian tubes, thickened and edematous, presented a chronic inflammatory response. A similar reaction was less marked in the appendix. The 3 cm. cyst as well as others associated with the peritoneal surfaces of the right fallopian tube and ovary had mesothelial linings.

The body of the uterus was received incised longitudinally. In this state its dimensions were 8 cm. in superior-inferior diameter, 8 cm. in lateral diameter, and 3.7 cm. in anterior-posterior diameter. A soft pink nodule not unlike early placental tissue,  $2\frac{1}{2} \times 2 \times 1$  cm., bulged from the cut surface of the myometrium at the fundus and occupied a portion of the exposed endometrial cavity, to which it then had access through the postoperative incision. On dissection this nodule was found to be a continuation of a branching, truncated mass of similar character, 7.5 cm. long and 0.1 to 1.5 cm. in diameter, ramifying throughout the myometrium of the fundus from cornu to cornu. It was soft and pink, separated readily from its myometrial bed, leaving a smooth surface without a definite capsule, and appeared throughout much of its course to be composed of a group of cord-like structures

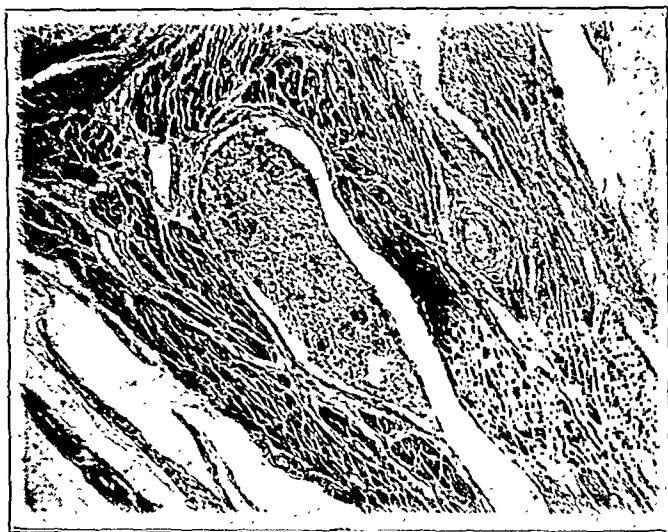


Fig. 3.—Cord of tumor tissue within a dilated vein.

having axes coinciding with those of the ramifications of the growth itself. A boggy swelling  $2\frac{1}{2}$  cm. in diameter at the left cornu was found to be occupied by a portion of the mass. On separating the appendages from the uterus, a soft, red, smooth, globular structure a few millimeters in diameter bulged from the cut surface of the broad ligament of the left side immediately beneath the isthmus of the fallopian tube. The peritoneal and endometrial surfaces nowhere were perforated by the growth. The endometrium was smooth, thin, and pink. The mass did not involve the lower half of the body of the uterus.

Microscopically, the branching truncated mass was composed essentially of conspicuous blood vessels which served as axes for a perivascular distribution of smooth muscle fibers. The blood vessels and surrounding muscle fibers constituted units which were grouped somewhat indistinctly into cord-like structures bordered by a loose edematous connective tissue stroma (seen in cross-section in Fig. 2). In many instances such cords, with a smooth thin mesothelial surface, occupied dilated venous paths (Fig. 3). Fusion of the neoplasm with adjacent myometrium after the manner of malignant neoplastic invasion was nowhere observed. The tissue was well differentiated. Many of the blood vessels serving as axes for the units had hyalinized walls; others were markedly dilated (Fig. 4). The muscle fibers about the blood vessels in most instances occupied a concentric relationship to the vessel; in other

instances they presented a radial arrangement. Inflammatory infiltrations of leucocytes and wandering cells were marked in some areas. The neoplastic tissue was found only in the fundus; several sections covering the circumference of the lower portion of specimen were free from the tumor.

At the present time, nearly fourteen months after operation, the patient is reported to be well and is working.

#### COMMENT

Superficially, the unusual ramified shape of the tumor suggests a malignant neoplasm. The ramifications, however, everywhere could be separated readily from the myometrium. For the greater part, they were not attached to their myometrial bed. Histologically, the well differentiated structure supports its benign nature. The absence of a compact circumscribed tumor and the soft pulp-like structure are unlike the usual myoma of the uterus, but not unlike an angioma. The tendency toward



Fig. 4.—Area in which dilated blood vessels constitute the most conspicuous feature of the tumor.

intravascular growth without being adherent to the vessel wall is seen occasionally in myomas.

#### SUMMARY

A uterine neoplasm having an unusual ramified distribution within the myometrium, regarded to be benign, structurally consisting of cords of perivascular groups of smooth muscle cells, with the blood vessels constituting the greater part of the bulk in some areas, is recorded, occurring in a patient having bilateral chronic salpingitis, and found incidentally at an operation performed for the purpose of relieving that condition.

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## ADENOSARCOMA OF BODY OF UTERUS

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TWO cases of an unusual variety of tumor occurred in the surgical material at the Roosevelt Hospital within a few months of one another. These were both polypoid tumors of the body of the uterus filling a considerable portion of the endometrial cavity, and in one case, dilating it very markedly. On microscopic examination both proved to be made up of a mixture of tissues including smooth muscle, myxomatous fibrous tissue, spindle-cell sarcoma, cartilage and an admixture of glands of the endometrial type but poorly developed and immature. This type of tumor was clearly described by Wilfred Shaw in 1928.<sup>1</sup> He collected from the lit-



Fig. 1.—Microphotograph of Case 1 ( $\times 70$ ). The admixture of gland-like spaces and cellular stroma containing cartilage can be observed.

erature thirteen cases, of which the earliest was reported in 1870. Shaw compared these tumors with the grape-like sarcoma of the cervix (*Sarcoma botryoides*), a much commoner tumor, which he found was also histologically a mixed tumor of similar composition and microscopically of the same variety. He also makes note of a third group of mixed tumors of this peculiarity of structure occurring in children in the vagina. This entire group of genital mixed tumors has a marked resemblance to the Wilms tumors of the kidney and Wilms himself in his monograph in 1900 compared the "*Traubiges Sarkom*" of the cervix to the mixed tumors of the kidney, considering them of similar embryonal development. The rarest of the tumors are those occurring in the body of the uterus and here, too, the age occurrence is markedly different from those occurring in the cervix or vagina. The ages given in the reported cases were as follows: 50, 49, 56, 62, 75 and 58. These cases all occurred after the menopause. Most, if not all of them, were polypoid, and Shaw considers that the structure differs from that of the cervical tumors largely because the limitation of the tumor to the endometrial cavity restricts the formation of multiple polypoid projections as in the grape-like sarcoma of the cervix. Another case of

mixed tumor of the body of the uterus was reported by Wolfe.<sup>2</sup> This occurred in a patient of fifty-five years, in conjunction with fibromyomas and was a polypoid tumor consisting mainly of myxomatous and cartilaginous elements. The case histories of the two examples here reported, follow:

Mrs. C. L. B., aged fifty-five, came to Roosevelt Hospital, September 17, 1930, under the care of Dr. H. C. Taylor. She had had four children, the last twenty-five years ago. In 1918 she was given radium treatment by Dr. Corscaden for an enlargement of the uterus which was considered a fibroid. After that, menstruation ceased. Her complaint on admission was backache, with some urinary symptoms, especially urgency. Operation was performed. The uterus was found much enlarged and a complete abdominal hysterectomy was done. The specimen was found to consist of a much enlarged uterus with tubes and ovaries with a combined weight of 1030 gm. On section the uterus was seen to have a much dilated cavity filled by a pedunculated mass measuring 15 by 12 by 10 cm. The surface was irregularly brown



Fig. 2.—Microphotograph of Case 1 ( $\times 200$ ). The stroma cells are large, with a mixture of round and spindle shapes. The epithelium of glands and cords is seen to be atypical. Mitotic figures are present.

and red with some erosion. The cut surface was soft, fibrous and fatty with many small cysts. A great deal of tissue was hemorrhagic and necrotic. The microscopic appearance was so similar to that of the second case that the descriptions are combined below. The postoperative course was uneventful. About six months after operation symptoms of partial intestinal obstruction developed. There was no palpable pelvic mass but the region was indurated. In spite of x-ray treatment to the pelvis, the obstruction became worse and the patient died during November, 1931. No permission for autopsy was obtainable.

The second case, Mrs. S. G., aged sixty-four, came to Roosevelt Hospital, under the care of Dr. W. P. Healy. She had had radium treatment nine years ago which resulted in menopause. In June, 1930, uterine bleeding began and continued until August. X-ray treatments were given in July and in September. Patient was examined under ether, on October 4, 1930, and a globular uterus was felt. On curetting, fragments were removed which on microscopic examination were reported as resembling necrotic fibroid. Operation was performed February 20, 1931, with the removal of the uterus and adnexa. The combined weight was 125 gm.; the uterine lumen was enlarged, being entirely filled by a yellowish red, fungating, pedunculated growth, attached to the fundus by a firm fibrous pedicle 2 cm. in diameter. There

was no encapsulation at the attached base of the tumor. The uterine wall was about  $1\frac{1}{2}$  cm. in thickness and seemed normal. The adnexa were negative. The subsequent course of this patient was uneventful and in January, 1932, eleven months after operation, she reported herself free of symptoms.

The histology of these two tumors was similar in all respects. There was no evidence of encapsulation and on the border between the tumor and the uterine wall invasion seemed to be taking place rather actively. There were numerous clefts and gland spaces lined by cuboidal or columnar epithelium, characterized by a frayed inner border and vesicular nuclei. Usually one layer of epithelium was present but sometimes the epithelium was heaped up and in some of the larger spaces secondary acini were formed. This epithelium showed mitotic figures and resembled adenocarcinoma of endometrial origin. The stroma was remarkable in its variety. Most

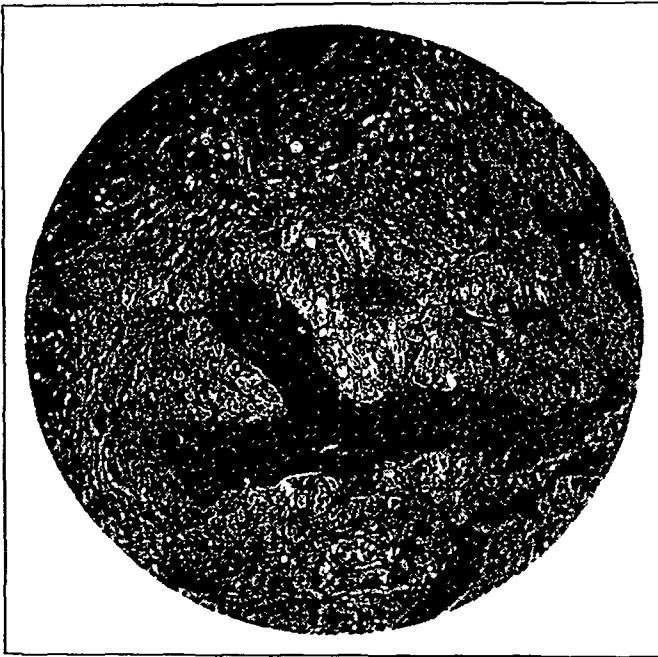


Fig. 3.—Microphotograph of Case 2 (x600). The section is through the pedicle of the tumor and the upper part of the section is myometrium which is being invaded by epithelial elements which here have the appearance of actively growing carcinoma.

frequent was a myxomatous appearance, with small cells resembling fibroblasts predominating, but in places the cells were large spindle cells often with giant nuclei, having every appearance of a rapidly growing sarcoma. In other foci the intercellular substance was of more solid consistency and small round islands of typical cartilage matrix and of smooth muscle were found. There were also large cells with eosinophilic cytoplasm and single or multiple nuclei which had the appearance of embryonal striated muscle. In some of the gland spaces a portion of the epithelium consisted of large cells with much clear cytoplasm and small central nuclei resembling keratinized epithelium.

These tumors are readily recognizable by their remarkable histologic structure and apparently form a special group which characteristically occurs in the postmenopausal period and causes enlargement of the uterus and bleeding. Apparently most of the tumors, if not all, judging by Shaw's report, are pedunculated intrauterine masses. Because of the invasive character of the growth, the malignancy must be fairly marked, and according to the previously reported cases, recurrence and metastases are to be expected. If comparison with Wilms tumors is justifiable, a



great deal should be expected of radiation therapy, since in this group, the radio-sensitivity is of high degree.

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## ARTIFICIAL PNEUMOTHORAX AND PREGNANCY WITH THE REPORT OF TWO CASES\*

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IT IS my privilege to present the following two cases of advanced pulmonary tuberculosis who have been treated successfully by artificial pneumothorax and who went through full-term pregnancies while under treatment.

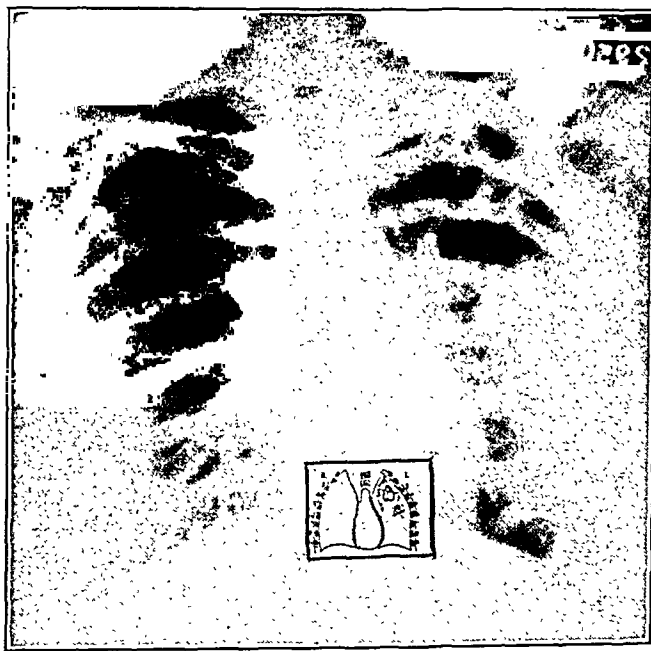


Fig. 1.—Case 1. Condition of lungs on admission to the sanatorium July 20, 1928. Infiltration, consolidation, and excavation in upper half of left lung. Sputum positive for tubercle bacilli. Note size of cavity.

CASE 1.—R. S., aged twenty-two, first came under my observation at the Eagleville Sanatorium on July 20, 1928, suffering with advanced active tuberculosis of the left lung, temperature 99.8°, pulse 96, sputum positive for tubercle bacilli. Clinically there were signs of excavation in the first interspace anteriorly, with râles extending to the fourth rib. The patient also complained of nausea and vomiting with pain over the right lower abdomen, and no menses for the past two months. These symptoms, however, received little consideration at the time and were believed to be due to probable ileocecal tuberculosis. The patient was placed on calcium chloride therapy intravenously and in due time the nausea and vomiting disappeared. During the first six weeks of observation, the temperature, cough, and expectoration continued to in-

\*Presented, by invitation, before the Obstetrical Society of Philadelphia, March 3, 1932.

crease in severity and the patient was losing steadily in weight. On September 1, 1928, artificial pneumothorax was instituted on the left side and almost immediately the patient began to show definite improvement. Temperature and pulse soon quieted down to normal, cough and expectoration was greatly reduced and tubercle bacilli disappeared from the sputum. The patient began to gain in weight and naturally felt greatly elated over the turn of events. On November 8, 1928, the patient called my attention to the fact that her abdomen was increased in size and made the suggestion that she was pregnant. Careful examination soon confirmed the diagnosis and for



Fig. 2.—Case 1. May 8, 1929, two months after giving birth to a healthy, male child while under artificial pneumothorax treatment. Note fluid level and collapse of left lung. The cavity although greatly reduced in size is still visible. In the diagram the uncollapsed part of the left lung is represented by the shaded area, the solid area indicates fluid. Sputum negative for tubercle bacilli.

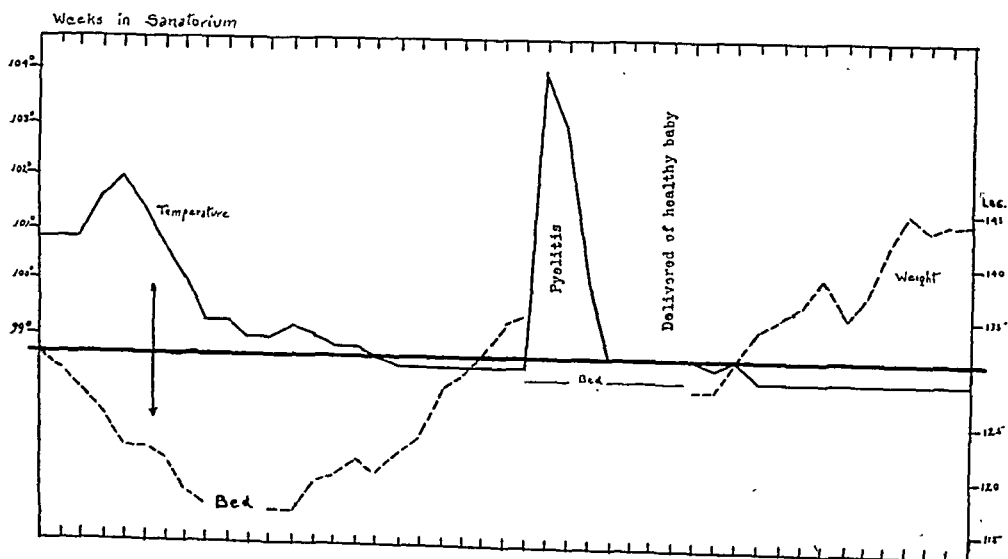


Fig. 3.—Case 1. Clinical course during stay in sanatorium. Admitted July 20, 1928, discharged July 16, 1929. Artificial pneumothorax to left lung (indicated by arrow) initiated September 1, 1928. Delivered of healthy, male child, March 4, 1929. Both mother and baby at the present time, March 24, 1932, enjoy good health. Mother still receives artificial pneumothorax treatment.

the first time it was realized that the patient was pregnant on admission and that the nausea and vomiting were not due to ileocecal tuberculosis as was first believed but to pregnancy. Of course, it was too late to interrupt gestation, and again the patient was in such splendid shape clinically, that she was advised to go through with it. Everything went along smoothly until January 10, 1929, when she suddenly developed a high fever of  $104^{\circ}$  with moderate pain in the right upper abdomen. A diagnosis of right sided pyelitis was established and the patient treated accordingly with satisfactory results. At the same time fluid appeared in the left pleural cavity which required several aspirations. On March 4, 1929, the patient delivered a healthy male child at the Jewish Hospital under the supervision of Dr. Walker. The convalescence was uneventful. Although the sputum became positive for a short time after the delivery, the tubercle bacilli again disappeared. The patient continued to gain in weight and strength and left my care as an arrested case of tuberculosis on July 16, 1929. A recent report from the patient stated that she was enjoying good health,

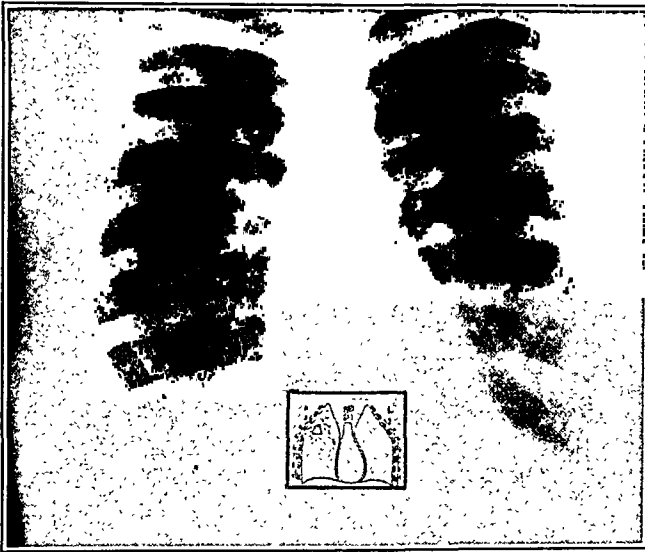


Fig. 4.—Case 2. Note the marked involvement of the right upper lobe with large cavity at the level of the fourth posterior rib. Sputum positive for tubercle bacilli.

that the baby was in fine shape, and that she was still continuing with artificial pneumothorax treatment.

It is highly probable that had I realized that this patient was pregnant when she first came under my care, she would have been aborted.

CASE 2.—I. G., aged twenty-four, first came under medical observation for tuberculosis in May, 1929, at which time she was known to be three months pregnant. Both x-ray and physical findings revealed softening and excavation of the right upper lobe. The sputum was positive for tubercle bacilli and clinically there was cough, expectoration, fever, and night sweats. During the two weeks prior to the diagnosis of tuberculosis, the patient had lost nine pounds in weight and was confined to bed. Because of the severe character and apparent acute onset of the tuberculous process a therapeutic abortion was performed on June 1, 1929, by Dr. Andrusier at the Howard Hospital, and the patient admitted to the Eagleville Sanatorium on June 14, 1929. My contact with the patient began on this date. The patient was still manifesting all the signs and symptoms of acute tuberculosis, and artificial pneumothorax to the right lung was instituted within a few days. In a short time, her temperature returned to normal, cough and expectoration practically disappeared, and her weight picked up

## Special Article

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### THE RÔLE OF FRONTIER AMERICA IN THE DEVELOPMENT OF CESAREAN SECTION

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WITH the present year the so-called modern era of cesarean section concludes its first half-century; and were one asked in what respect obstetrics has advanced most conspicuously during these five decades, one might fittingly point to the revolutionary changes which have occurred in the indications, the technic, and the prognosis of the cesarean operation. Throughout the greater part of the nineteenth century, cesarean section was the most fatal of surgical procedures. In Great Britain and Ireland, the maternal mortality from the operation had mounted in 1865 to the appalling figure of 85 per cent. In Paris, during the ninety years ending in 1876, not a single successful cesarean section had been performed. The results in Germany, Austria, and Italy were so poor that the newly introduced operation of Porro, which included hysterectomy as well as removal of the child, was succeeding the old and almost universally fatal cesarean section; the Porro procedure, it was claimed, saved more than half of the women subjected to it. As late as 1887, Harris noted that cesarean section was actually more successful when performed by the patient herself, or when the abdomen was ripped open by the horn of an infuriated bull. He collected nine such cases from the literature with five recoveries, and contrasted these with twelve cesarean sections performed in New York City during the same period, with only one recovery. In the face of such results, it is not surprising that many obstetricians of the nineteenth century doubted the wisdom of ever resorting to cesarean section, and predicted that the operation would shortly lapse into desuetude.

The turning point in the evolution of cesarean section was clear-cut and decisive. It was the appearance in 1882 of a monograph by Max Sänger, then a twenty-eight-year-old assistant of Credé in the University Clinic at Leipzig. The title of the work, "*Der Kaiserschnitt bei Uterusfibromen nebst vergleichender Methodik der Sectio Caesarea und der Porro-Operation*," scarcely suggested its real purpose, which was to recommend in cesarean section the routine employment of carefully placed uterine sutures. "The salient consideration in the proposed improvement of the classical cesarean section," he urges, "is without doubt the treatment of the uterine wound"; and through two hundred pages he evolves, amplifies and substantiates this same theme. The history of the uterine suture, the advantage of the buried uterine suture, the best material for sutures—these were a few of the many aspects of the subject which received detailed attention. In particular, Sänger deprecated the growing tendency to abandon the old classical cesarean section in favor of the new Porro procedure, since he believed that careful coaptation of the uterine wound with sutures would obviate all difficulties and permanently establish the superiority of the older operation. Such views were new, for neither in Europe nor in England had uterine sutures been considered necessary. His opinions were at variance, moreover, with the dictates of the most experienced operators of the time—and, let us remind ourselves, Sänger's experience had been limited to but one successful case. His contentions, however, were supported by

such carefully documented evidence, and his facts marshalled in such a logical and convincing manner, that the justice of his claims was apparent. Confirmation of his convictions followed quickly. Within a few years uterine suture was generally recognized as an indispensable part of cesarean section and forthwith the modern operation came into being.

The long neglect of so simple an expedient as uterine suture in cesarean section was not the result of oversight but was due to a deep-rooted belief that sutures in the uterus were superfluous as well as harmful. In 1770, Andre Levret, the foremost obstetrician of eighteenth century Paris, had taught that uterine sutures in cesarean section "were not only prejudicial but were absolutely useless because of the prodigious contractions which the uterine muscle undergoes following delivery." This view that sutures would cut through the uterine muscle and thus defeat their



MAX SÄNGER  
1853-1903

own end became widespread and was reflected a hundred years later in the unique work of the Italian surgeon, Silvestri, who sought to obviate this untoward result by employing elastic suture material. In 1874 he and his assistant, Veyer, reported two cases of cesarean section in which rubber bands were used for suturing the uterus. Another compelling argument against the use of uterine sutures was the copious suppuration which followed the suturing of abdominal wounds, a fact which naturally deterred surgeons from hazarding similar procedures in the uterus. In the main textbooks of the period, uterine suture was rarely mentioned, and, if so, but incidentally. Thus, Blundell, in his "Principles and Practice of Obstetric Medicine," published in 1840, dismissed the subject with the remark that "sutures to the uterus have not hitherto been in general employ." Similarly, Caseau, in his "Traité théorique et pratique de l'art des accouchements," which was enjoying wide popularity even as late as Sanger's time, commented briefly that "the uterine wound needs no treatment other than to keep it clean."

In other words, throughout the greater part of the nineteenth century, the uterine suture in cesarean section had been in general disrepute. It is true that, in a few isolated cases, it had been used both in Europe and in England, but these instances were not at all illustrative of Säger's conception, for in them sutures had been employed usually to stop bleeding rather than to unite the wound; as Säger points out, they were really ligatures. Thus, in the earliest recorded case of cesarean section in which uterine sutures were used, that of Lebas of Mouilleron, reported in 1769, three sutures were inserted, but avowedly for the sole purpose of controlling dangerous hemorrhage. Even this use of uterine suture, however, was so rare that Hasse, in 1856, could find in the literature only six cases in which uterine suture had been employed; and in general it seems clear that at the time Säger's monograph appeared, neither Europe nor England had had any appreciable experience with this procedure. If, now, in conjunction with this fact, it is also recalled that Säger's own experience with the uterine suture in cesarean section had been limited to one case, the question arises: whence came Säger's idea? What were the sources of that carefully documented evidence in favor of the uterine suture? Who were his forerunners? The answer to this question Säger, himself, states frankly and without reserve. As we have seen, his predecessors were certainly not his colleagues in the sophisticated medical centers of Europe, but were—oddly enough—certain pioneer surgeons working in the outposts of the American frontier. And, without wishing to detract in the slightest from the greater credit due to Säger, it is the purpose of this article to recall the almost forgotten contributions of these Americans to cesarean section.

The rôle of nineteenth century America in the development of cesarean section was two-fold. It comprised, in the first place, the introduction and the perfection of the silver wire uterine suture, which, as Säger later pointed out, constituted a turning point in the evolution of the operation; it consisted, secondly, in demonstrating the importance of that axiom of modern obstetrics, namely, cesarean section to be safe, must be done early in labor.

The conception and development of the silver wire suture in cesarean section was wholly an American achievement. In December, 1852, Frank E. Polin, a well known surgeon of Springfield, Kentucky, was consulted in the case of a certain Mary Brown, who had become exhausted from forty hours of labor, the dystocia being due apparently to a hydrocephalic child. Polin performed a cesarean section and closed the uterine incision with silver wire sutures; the patient survived, later bore two infants spontaneously, and was still in good health thirty years later. The details of the operation are scantily reported, and just what prompted Polin to employ sutures in the uterus, and particularly silver wire sutures, is not clear. It is significant, however, that in the January preceding Polin's operation, there appeared the celebrated paper of J. Marion Sims on the use of silver wire sutures in vesicovaginal fistula, and, although Sims did not mention the use of silver wire in cesarean section, it appears that his general idea bore fruit at the hands of the Kentucky surgeon. Polin did not record his case in the literature so that during the ensuing decade and a half, his experience was apparently forgotten. Between the years 1867 and 1880, however, uterine sutures were employed in sixteen cesarean operations in the United States, and in nine instances, at least, the material used was silver wire.

These early American surgeons were correct in believing that the silver wire suture offered them certain peculiar advantages in cesarean section. In the first place it did not require removal. As Sims himself had demonstrated in various abdominal operations, silver wire could be left in the tissues indefinitely as an innocuous buried suture with "no inflammation, no suppuration, no cutting out of sutures, no gaping or retraction of flaps, and therefore no necessity for disturbing

TABLE I. TABLE SHOWING THE EARLY AMERICAN CASES OF CESAREAN SECTION IN WHICH UTERINE SUTURES WERE EMPLOYED  
(Translated from Slinger)

CASE NO.	DATE	OPERATOR	AGE AND RACE	INDICATION FOR OPERATION	LENGTH OF LABOR, CONDITION OF PATIENT	KIND AND NUMBER OF SUTURES	OUTCOME MOTHER CHILD
1	1852	Frank E. Polin	36 White	Hydrocephalus	40 hours. Exhausted	Silver wire sutures	Lived
2	1867	T. Beers-Townsend	16 Black	Contracted Pelvis	62 hours	3 Hemp sutures. Also 5 ligatures	Lived
3	1867	D'Aquin and Brickell	23 Creole	Stricture of Cervix and Vagina	10 days. Restless. Pulse 144	6 silver wire sutures	Lived
4	1869	Sager	35 White	Contracted Pelvis (Dwarf)	9 hours. Sick. Has always used crutches	4 silver wire sutures	Died
5	1870	Palul de Marmon & Rodenstein	40 White	Contracted Pelvis	44 hours. Exhausted	1 uterine suture	Lived
6	1870	T. A. Foster	40 White	Eclampsia	2 weeks (?). Having convulsions	10 silk sutures	Died
7	1871	J. U. L. Quackenbush	30 White	Contracted Pelvis (Dwarf)	3 days. Exhausted	2 silver wire sutures	Died
8	1872	E. C. Griffin	37 White	Fibromyomata	No definite pains but exhausted	1 silk suture	Died
9	1874	T. Gaillard Thomas	30 White	Fibromyomata uteri	Few hours in labor. Attempts at version and craniotomy	Silver sutures	Died
10	1875	Jones & Kline	35 White	Sacral exostosis (Dwarf)	38 hours. Exhausted	1 silk suture	Lived
11	1875	S. S. Lungren	29 White	Contracted Pelvis	Few hours. Membranes intact	5 silver wire sutures	Lived
12	1876	O. B. Barber	17 White	Contracted Pelvis (Dwarf)	Early operation	3 silver wire sutures	Lived
13	1877	E. W. Jenks	24 White	Contracted Pelvis	7 days. Exhausted	4 silver wire sutures	Lived
14	1877	G. E. Walton	19 White	Shoulder presentation	Long labor. Already sick; abscess in flank; cough; diarrhea. Attempt at forceps	1 silver wire suture	Died
15	1878	R. G. Curtin	20 Black	Contracted Pelvis (Dwarf)	24 hours. Membranes intact	7 carbolized catgut sutures	Died
16	1880	S. S. Lungren	34 White	Patient same as in Case No. 11	Contracted pelvis. Previous cesarean section	3 silver wire sutures	Lived
17	1880	M. Baker	34 White	Fibromyomata uteri	60 hours	9 horse-hair sutures 4 silk sutures	Lived

the dressing till all is firmly united and permanently well." This Utopian picture of wound healing was in welcome contrast to the prolonged ordeal of suppuration and sloughing which in those days followed the use of silk, linen and hemp. Particularly in cesarean section, in those few early cases in which uterine sutures had been employed, the irritation and suppuration caused by nonmetallic sutures were so intense that the early removal of the stitches was thought imperative. To this end various expedients had to be devised. Sometimes the ends of the sutures were left long and were allowed to extrude from one end of the abdominal wound; more frequently the lower angle of the abdominal incision was intentionally left open so that the uterine sutures might later be inspected and fished out by sight; some authors even advised that the ends of the sutures be brought out through the vagina and subsequently withdrawn through that outlet. This difficulty in regaining the uterine sutures was, indeed, one of the chief obstacles to their general use. Furthermore, the prevalent practice of removing the uterine sutures on the third or fourth day postpartum prevented their serving any real purpose in effecting permanent coaptation of the uterine edges, and it is not surprising that subsequent autopsy studies on such cases revealed conditions identical with those in which no sutures at all had been employed. In patients who died before removal of the silk or linen sutures, it was commonly observed either that the stitches had cut through the tissues or that the knots had slipped, and in either event the sutures were found dangling loose in the suppurating wound. But all these difficulties, which had seemed so inseparably associated with the insertion of nonmetallic material into the uterus, promised to vanish with the advent of silver wire.

The pertinent facts concerning the seventeen American operations in which uterine sutures were used, are listed in the accompanying table. As is noted in the legend, the table is a translation of one occurring in Sanger's monograph. That Sanger saw fit to collect and tabulate these cases in such detail and that he gave them such prominence in his study, is clear enough evidence of the important role they played in the evolution of his hypothesis. It may also be noted that no more convincing proof of Sanger's wholehearted fairness and generosity could be desired than this enthusiastic tribute to his American predecessors. The maternal mortality among the sixteen cases in which the suture material was specified, was 50 per cent, a figure decidedly better than that reported in England for cesarean section and slightly lower than that recorded by the most experienced surgeons on the Continent. Most of these patients had been in labor for days; all of them had been subjected to repeated and lengthy vaginal examinations and in many instances, vain attempts had been made to deliver the women by forceps or craniotomy before the cesarean operation was undertaken. In view of the desperate condition of the patients, indeed, it seems doubtful whether classical cesarean section today would offer such a group a much better outlook. Sanger, however, was interested not so much in studying the gross mortality rate as in the correlation between the maternal outcome and the number and kind of uterine sutures which had been employed; and on the basis of the American statistics he was able to show that the prognosis in cesarean section improved in proportion to the number of uterine sutures used, particularly in those cases treated with silver wire.

It is true that in some of the earlier cases in the group, uterine sutures were employed primarily for hemostasis, but even in these cases, it soon became evident to the operators that the sutures also fostered better wound healing, prevented the escape of lochial fluids into the peritoneal cavity and decreased the likelihood of puerperal peritonitis. Thus, in the earliest of the American cases to be recorded, that reported by Brickell in 1869, the several advantages of the uterine suture are clearly set forth:



"A most important observation was that of the failure of the uterus to contract fully on its own cavity after the ovum was removed. Indeed, the organ had to be freely manipulated to make it contract even moderately. Not only did the blood continue to flow freely from the large wound inflicted, but one side of the flaccid organ absolutely fell in, and had to be lifted up to pass the sutures. . . .

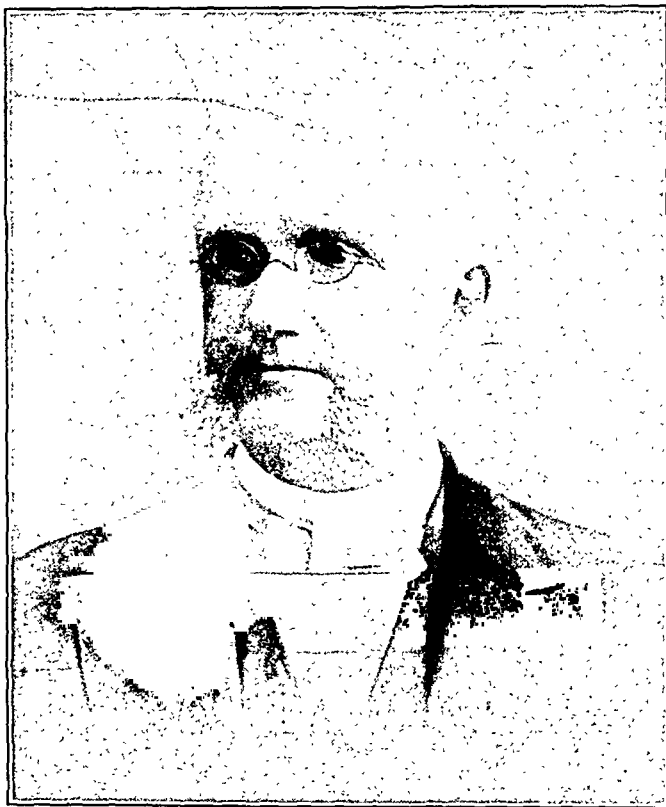
"The remedy for this hemorrhagic condition is, so far as I am aware, novel. With the exigency before us, there could not be a doubt in my mind as to the remedy, and it is seen that not only was the hemorrhage promptly arrested by close adaptation of the cut surfaces of the uterus but the collapsion of the organ was in this way relieved, and the wires have up to this moment proved wholly innocuous. I find in this part of the operation the most interesting point of all. I have long been of the opinion that in all probability the majority of deaths from cesarean section were the result of bleeding from the uterine walls into the cavity of the abdomen—the bleeding itself depressing the woman, and the effused blood lighting up peritonitis. Moreover, I have thought that concomitant with this bleeding was the gaping condition of the wound, the consequent absence of healing by first intention, and the strong invitation to metritis and septicemia. I have often resolved in my own mind to sew up the uterus in case I should be called on to operate, no matter how well it might contract at the time of operation; and on the ground that even the most vigorous uterus, after a normal delivery, is liable to expand and bleed, and in case of the section being made and our sewing up the abdomen over a womb we see to be well contracted, we cannot say that such secondary expansion will not occur; indeed, I contend that we have the right to expect the shock of operation to produce such expansion, and if the organ be not secured by sutures the result must ever be disastrous. I am satisfied that it may be theoretically and practically asserted true surgery to apply the metallic suture to the uterus in all such cases. The innocuous nature of the metallic suture is every day proved in surgery, and there can be no reason for apprehending the danger from its application in every case of cesarean section."

To other American surgeons, the study of the uterine wound, when examined possibly years later at autopsy or at a subsequent operation, afforded further evidence of the value of the uterine suture. Thus, in 1880, S. S. Lungren, a Toledo surgeon, had occasion to perform a cesarean section on a patient who had undergone the same operation five years before. In commenting on the condition of the uterine scar, Lungren observed that "contrary to expectations, no adhesions were found between the uterine and abdominal walls. The uterus was freely movable. . . . The silver sutures were seen under the peritoneum as bright as when placed there five years previously." The theoretical advantages of the uterine suture were likewise clear to Lungren, as the following passage shows:

"... the sutures being introduced partly through the uterus, the peritoneal surfaces are retained in contact until union takes place, and all danger of escape of (lochia) fluids averted. This method of introducing the sutures is the more necessary, for as soon as the incision is made and the contents of the womb extracted, eversion of the lips of the wound takes place to a great degree, the external edges being bevelled off; and as soon as absorption commences below in the interior, the slit would be enlarged, affording ready exit to the fluids. To obviate such results was the aim in the introduction of sutures."

Another zealous advocate of the uterine suture in cesarean section was Charles F. Rodenstein of Westchester, New York, who as early as 1870 stated that "the appli-

cation of uterine sutures after every cesarean section will probably diminish the rate of mortality attending that operation." His view was founded on an examination of the records of four hundred cesarean operations performed since the beginning of the nineteenth century. In studying the postmortem findings, he was particularly struck with the frequency of such statements as these: "the uterus was found open"; "the edges of the wound gaped"; and "the uterine incision did not close." He reached the inevitable conclusion that the majority of fatalities following cesarean section resulted from the escape of blood and lochia into the peritoneal cavity; but, he advised, "by closing the wound with sutures, the danger of such unfortunate occurrences may be prevented."



ROBERT P. HARRIS  
1822-1899

The papers of Brickell, Rodenstein, Lungren and others, thus, leave little doubt as to the genuine enthusiasm with which many American surgeons pleaded for the use of the uterine suture in cesarean section. Some years before the appearance of Säger's work, these men had appreciated the whole rationale of the uterine suture, had shown by their results its many practical advantages and had advocated its employment in every cesarean operation. Yet, it is questionable whether any of their individual reports, which were often brief and appeared for the most part in obscure medical journals, would ever have attracted European consideration if it had not been for the exhaustive studies of Robert P. Harris of Philadelphia, who must be regarded, at least so far as Europe was concerned, as the spokesman for the American surgeons. With unremitting energy he searched the whole country for every case of cesarean section which had been performed, tabulated the circumstances and details of each operation and between the years 1872 and 1881 published

six lengthy statistical surveys covering the whole field of cesarean section in the United States. As Dr. Howard A. Kelly has noted, Harris was the most prominent obstetric statistician this country has ever known, his writings attracting attention both in Europe and in England. Indeed, one of his statistical studies on ectopic gestation involved him in an imbroglio with Lawson Tait, who called him a "library surgeon." Other papers of Harris appeared in German and Italian medical periodicals. The influence which his writings on cesarean section exerted in European circles is amply attested by the fact that in Sanger's monograph his name appears more often than that of any other author, Zweifel, the leading German authority on cesarean section, not excepted. If it be granted then, that Sanger's acquaintance with cesarean section in the United States was derived from Harris' papers, what did the German author learn there concerning the American attitude toward the uterine suture? Did Harris recommend its routine employment? This question is important, since its answer explains Sanger's honest belief that he was the first to advise the routine use of this procedure. Harris did not advocate the insertion of uterine sutures in every cesarean section, but only in certain selected cases. In general, he was inclined to reserve his opinion, and as late as 1878 remarked that "the experience of our country is as yet entirely too limited to determine whether the employment of the uterine suture is, or is not, an improvement in the method of operating. . . . The fear has been that sutures in the uterus would greatly increase the danger of peritonitis; but the dangers to be encountered by using them are often not to be considered, in view of the greater risks in endeavoring to avoid their employment. In atony or hemorrhage at the time of the operation, there can be no question as to the better safety of the suture." It was thus, with faint praise, that the spokesman for the American surgeons reported his country's experience with the uterine suture in cesarean section.

But upon another important issue in cesarean section, Harris took a much firmer stand and was adamant in his insistence that cesarean section to be safe must be done early in labor. This one unifying theme runs throughout his writings; and whether he deals with "cattle-horn cesarean section" on the plains of the West or with the results of cesarean section in the hospitals of New York City, he invariably finds evidence in support of the "timely operation." This teaching that cesarean section be performed early in labor has since proved to be the watchword to success in the operation, and as it was first announced clearly by American surgeons, it deserves recollection as one of the creditable contributions of this country to obstetrics.

It must be noted, however, that the advisability of early operation had already been suggested, at least, by Thomas Radford of Manchester, England. In 1865, this author analyzed all the recorded cases of cesarean section in Great Britain and Ireland and, after finding that the maternal mortality of the series was 85 per cent, advanced the opinion that better results might be obtained if the operation were performed earlier in labor as a procedure of choice rather than being delayed until it became one of necessity. He cites no figures to substantiate his opinion, however, and summarizes his views in the following two sentences: "Notwithstanding all the preexisting dangers of cesarean cases, several recoveries have taken place. The favorable terminations ought to encourage us to hope, and indeed ought to inspire us with confidence, that if the operations were earlier performed, and on a different class of subjects, it would be attended with infinitely more success." Until the close of the nineteenth century in fact, it was still held that the most favorable time for performing cesarean section was at the end of the first stage of labor, an attitude prompted by the belief that the hemorrhage incident to incising the uterus would be minimized if the uterine muscle was in a very active state of contraction.

To perform cesarean section before the advent of labor was thought to be particularly dangerous and even after Bar of Paris, in 1888, had reported favorable results in cesarean operations done at this time, the practice was still regarded as hazardous. In view of this doctrine, the natural tendency to delay so dangerous an operation until it was clearly imperative met with general approval, and cesarean section remained an operation of last resort.

The first of Harris' papers attacking the evils of delay in cesarean section appeared in 1871, and from the beginning the author pleaded with compelling logic and vigor in behalf of the early operation. Some of the evidence upon which he based his contentions was unique. Thus, he called to mind, in the first place, that the first cesarean section to be performed upon a living woman was said to have been done in 1500 by a Swiss sow-gelder upon his wife, with happy results both for mother and child. The first authentic operation in the British Isles was one performed by a common midwife, Mary Dunally, upon a certain Alice O'Neal of Ireland, in 1739. The outcome was successful, although in the next thirty-seven cesarean sections performed by physicians in Great Britain between 1739 and 1845, only three women survived. The first recorded cesarean section in the United States was performed in 1822 by the patient herself, a fourteen-year-old quadroon servant, who made an "L" shaped incision through the abdominal wall and uterus while lying in a snow bank; she also recovered. Having noted these facts, Harris then extended his observations to more recent years and in studying the conditions in this country found that the mortality from the operation actually seemed to increase in direct proportion to the skill of the surgeon and the excellence of his equipment. For instance, the highest death rate was reported for New York City and State, where among twelve women subjected to cesarean section by surgeons and surgical accoucheurs of considerable eminence, but one mother survived. Some of the best results, on the other hand, came from the prairies of the West, where, as we have already noted, the outcome was often favorable even in cases in which the abdomen had been ripped open by the horn of a bull. Particularly gratifying were the figures reported from the plantations of Louisiana, where the mortality from the operation among the slave women was but twelve and one-half per cent, although in New Orleans three-quarters of the mothers subjected to cesarean section had died. Similarly, in the farm houses of Indiana, Ohio and Kentucky, the operation was frequently successful. From Mexico, Cuba, Jamaica, Martinique and Tortola, came reports of eight cases of cesarean section with seven maternal recoveries. Indeed, it seemed that the farther from civilization the operation was done, the greater the likelihood was of success. The truth of this paradox Harris emphasized even more strikingly by showing that in "the open country" of the United States, the maternal mortality from the operation was but 38 per cent, while in the towns and villages it was 65 per cent and rose still higher in the large cities. What could account for these inconsistencies? Were surgical skill and hospital care of no avail? Of course they were, answered Harris, but they could not offset the dangers caused by delaying the operation; and it was in the cities, Harris showed, that delay was most common, the delay which so often comes from multiplicity of counsel. In the open country, on the other hand, either by accident or by the boldness of ignorance, the operation was performed early in labor while the patients were still in good condition, and hence it was successful. Certainly, in the case of "cattle-horn cesarean section," an accident that usually occurred before labor had even begun, such an interpretation was the only available one. Today, we might be inclined to supplement Harris' explanation with other factors, but in the main his tenets were sound; it was the countryside, the American frontier, which first demonstrated the safety of cesarean section.

Other types of cases were likewise grist for Harris' statistical mill and afforded

additional evidence in favor of the "timely" operation. Thus, in cases of rupture of the uterus during labor, he found that abdominal delivery was a relatively safe procedure. One might think that this operation, performed after rupture of the uterus in order to remove the fetus and its secundines, would turn out to be a more severe and fatal operation than cesarean section, but such was not the case, and, as Harris pointed out, for two reasons. In the first place, where rupture of the uterus occurred, the necessity for a prompt operation was generally recognized both by the accoucheur and the surgeon; and secondly, the subjects of rupture were as a general rule in better condition than those who eventually subjected themselves to cesarean section. Still more convincing were the lessons which Harris drew from another class of patients; namely, those upon whom cesarean sections had been repeated. In such cases, the circumstances which had necessitated the previous operation usually made it clear that a natural labor would be impossible and accordingly cesarean section was decided upon at an early date and carried out either at the onset of labor or shortly after. Here, then, was a group of cases which exemplified *par excellence* the teachings which Harris had advanced, and, as he had predicted, the results were startling. Among nineteen operations performed on nine women, there were only three maternal deaths. By adding to these American statistics those of similar cases from other countries, it was shown by Lungren that a total of one hundred and nineteen operations had been done on forty-eight women with only eight maternal deaths, or in other words, with a maternal mortality of less than seven per cent, which in 1881 was an unheard of figure. So, by utilizing cases of various sorts from many sources, Harris, Lungren, and other American writers made it plain that cesarean section in this country was in general attended by a maternal mortality of about fifty per cent, but that when the operation was performed during the first twenty-four hours of labor, the mortality fell to twenty per cent, while in operations done at the onset of labor, as in repeated cesarean sections, it dropped to a level below ten per cent. It is not surprising, therefore, that Harris was such a fervent champion of the "timely" cesarean operation and that, somewhat before Sanger, he urged its superiority over the Porro procedure in the following words:

"I do not feel that there is the same demand for a change in the United States, where the old operation has had so large a measure of success, especially when performed in a few hours after the commencement of labor. Let the cesarean operation be one of election and anticipation as the most successful Porro sections have been; let it be performed under carbolic spray; the abdominal cavity thoroughly cleansed from blood and amniotic fluid; the uterine wound, if need be, closed with silver wire; let a drainage tube be introduced, and the parts be dressed according to the methods of Keith and Lister; and we shall expect in this country to save more cases than has been done, in proportion, in any European hospital, under the Porro method."

However, in attempting to evaluate the accomplishments of these nineteenth century Americans, it is important not to lose historical perspective. After all, it was Sanger's study which dealt the final blow to the old cesarean methods. At a time when all of Europe was clamoring for the radical Porro procedure and England was turning to craniotomy, he proved to his colleagues on undeniable grounds the superiority of the conservative cesarean section; he not only advocated the routine use of aseptic uterine sutures, but showed in the minutest detail how to insert them; and by combining the scientific principles of wound coaptation with full Listerian technic, he created at one stroke the modern operation. But, to have furnished the supporting data for Sanger's hypothesis, to have devised and demonstrated the earliest successful type of uterine suture and to have shown for the first time the

immeasurable value of the "timely" operation—these were certainly no mean achievements and may be recalled with pride as contributions of frontier America to cesarean section.

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**Walther**: The Value of Bisection of the Superior Hypogastric Plexus in the Treatment of Pelvic Neuralgias. Bruxélles-méd. 10: 29, 1929.

The superior hypogastric plexus innervates essentially the tubes and uterus but it does not supply the ovaries. For this reason section of this plexus leaves intact the sensibility of the ovary. The plexus is composed almost entirely of sensory fibers and its ablation has no effect on the muscular contractibility of the uterus. Walther has practiced section of this plexus on 14 patients. In eleven the complaint was that of severe dysmenorrhea, while in three the pain was persistent and intermenstrual in type. Twelve of the patients were cured or greatly relieved while only in two cases there was no relief. One of these failures was explained on the basis that the pain was ovarian in origin while in the other the uterine pain was relieved but a coccygodynia persisted.

The operation is indicated in cases of metritis or chronic painful salpingitis where medical treatment has failed and where because of the patient's age castration is to be avoided. It is not indicated in pain of ovarian origin.

THEO. W. ADAMS.

# American Journal of Obstetrics and Gynecology

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GEORGE W. KOSMAK, M.D., EDITOR

HUGO EHRENFEST, M.D., ASSOCIATE EDITOR

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## Editorial Comment

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### THE MODERN CESAREAN OPERATION

A HALF century has passed since Max Sänger published in Leipzig his monograph on the suturing of the uterus after cesarean section. We must regard this as one of the most outstanding contributions to obstetric surgery. It is therefore fitting for the JOURNAL to take note of this anniversary year, by publishing in the present issue a paper by Dr. N. J. Eastman, of Johns Hopkins, in which the interesting fact is brought out that certain pioneer surgeons of America furnished the basis for Sänger's improved operation, as he himself duly acknowledges. And it is to the files of the predecessor of the AMERICAN JOURNAL OF OBSTETRICS AND GYNECOLOGY that many of these noteworthy contributions to the literature were made. We are pleased therefore to round out this record by giving space to the interesting article of Dr. Eastman in the current issue.

Perhaps the occasion should call forth a word of comment on the acceptance of this obstetric operation, no longer as a procedure solely of necessity, but rather as one of choice. It is a far cry from the days of Sänger, when by mere suture of the incised uterine wall, the dangers of the operation were largely reduced. And yet the element of risk has not been completely eliminated, for we still find a considerable mortality associated with cesarean section as compared with surgical laparotomies in general. Where must we seek the cause? Is it due to lack of skill, of failure to observe proper indications, or have we substituted without proper justification, a procedure purely surgical, for others more essentially obstetric in their underlying requirements? Cesarean section is not difficult of execution by a well trained surgeon, it offers an easy solution of many obstetric problems and its performance is always attended with a certain theatric glamor. But the mortality rate which has accompanied cesarean section even in recent years, except in the best ordered clinics, shows that the operation is not as free from danger as its enthusiastic advocates would lead

us to believe, and that we must continue to seek, as Sanger did, the means to place it on a firmer basis, with due regard to the indications for its performance and the qualifications of the operator. Perhaps the success of such efforts will show a lowered mortality and morbidity rate during the next half century, with consequent greater safety to the mother and that such progress may be recorded with justified pride in a future issue of this JOURNAL, should it survive to commemorate the hundredth anniversary of the Sanger operation.



# Society Transactions

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## AMERICAN GYNECOLOGICAL SOCIETY

### FIFTY-SEVENTH ANNUAL MEETING

Quebec, Canada

MAY 30, 31, AND JUNE 1, 1932

*(Continued from November issue.)*

**Anterior Pituitary Lobe and Genital Function, Dr. Bernhard Zondek, Berlin, Germany. (By invitation.) (See page 836 for original article.)**

#### DISCUSSION

DR. ROBERT T. FRANK, NEW YORK CITY.—Recently I have preferred the Friedman modification of the pregnancy test as it can be used with mature animals, namely, rabbits. Isolation of the animals is not important and even if by accident a pregnant animal should be used superovulation is so strikingly superimposed upon the ovary that the test is likewise quite characteristic. The ovary macroscopically shows large blood spots, more readily recognizable than in the original Aschheim-Zondek test. In some 500 cases we have been able to find correct results in 90 per cent within twenty-four to thirty-six hours, meaning that thereby no positive results had been negated by the clinical history thereafter, but a certain number which I did not count in this percentage have at first proved negative and later, on repetition of the test, showed positive. We were able to recognize three cases of obscure tumors of the lung by the pregnancy test, which was positive, as chorioepitheliomata.

As regards the possibility of two hormones, mentioned by Prof. Zondek, we believe that there is really one hormone only, which produces both the follicle growth and the luteinization, and that this is a quantitative response.

Our attempts to duplicate Zondek's work on tumors I must say was disappointing. We did not study more than 30 cases but the results were so discordant that we stopped this work.

**Consideration of a New Viewpoint on the Etiology of Renal Tuberculosis in Women, Dr. Guy L. Hunner, Baltimore, Md. (See page 706, November issue.)**

#### DISCUSSION

DR. JAMES W. DUNCAN, MONTREAL, CANADA.—The technic employed by the essayist is of course different from that which is used by the majority of us. Dr. Hunner uses a much larger catheter. One wonders sometimes if the "hang," sensed by the speaker, may not at times be due to peristalsis in the musculature of the ureter excited by the irritation of the catheter.

DR. JOHN A. SAMPSON, ALBANY, N. Y.—I would like to ask whether Dr. Hunner uses the indwelling catheter for the purpose of maintaining drainage? If so, how long does he let it stay in and with what results?

DR. HUNNER (closing).—Dr. Rushmore spoke of the necessity for tests of function. That is one of the evidences that we are dealing with obstruction, the great in-

crease in phenolsulphonephthalein output after we give the patient better kidney drainage. I appreciate fully the skeptical attitude that most men have had toward each of my tradition-breaking suggestions. There was great opposition when I first proposed the drainage methods for hydronephrosis and for pyelitis, and later for patients suffering with stone, and still later for the cases of essential hematuria. I think men are coming to appreciate more and more the great value of drainage for all of these conditions, and I believe that we are going to learn to use these drainage methods in our selected cases of tuberculosis of the kidneys.

We do not use an indwelling catheter in these cases but simply depend upon repeated dilatation of the stricture at ten day intervals. The indwelling catheter is most valuable in some critical cases of pyelitis of pregnancy, and in some acute surgical conditions when we are trying to tide the patient over for a favorable time to operate. I have left an indwelling catheter for as long as three weeks, irrigating the kidney twice daily with 1 to 5000 silver nitrate solution.

**Chemical Changes in the Parturient's Blood, Dr. H. Siedentopf, Leipzig, Germany. (By invitation.) (See page 696, November issue.)**

#### DISCUSSION

DR. OTTO H. SCHWARZ, St. Louis, Mo.—I believe the work of Dr. Siedentopf may explain some of the cases of shock that take place after delivery.

In normal pregnancy we used to speak of a mild acidosis. This has been shown by Ward and Peters to be due to an alkali deficit, the sodium ion being most diminished. During a long labor, the patient receives little or no nourishment. Organic acids, both ketone bodies and lactic acid can accumulate, and it is reasonable to assume that a condition of acidosis could occur just at the time of delivery. The remarkable thing in Dr. Siedentopf's figures, is the transitory nature of this acidosis, the return to normal after labor being very prompt.

**The Influence of Sex Hormones on the Reticuloendothelial Cells of the Uterus, Dr. C. Frederick Fluhmann, San Francisco, Calif. (By Invitation.) (See page 654, November issue.)**

#### DISCUSSION

DR. JAMES R. GOODALL, MONTREAL, CANADA.—It is a very singular thing that oftentimes for years a course of treatment is adopted without knowing the real cause of the beneficent results which follow. Reticuloendothelial cells, that is a large name for a small cell, and we speak of them as macrophages or macroblasts, are not restricted to the uterus alone. They can be called forth in any part of the body. If an irritant is introduced into the abdomen or the blood of the patient, within twenty-four hours the reticuloendothelial cells are present in very large numbers. It is generally conceded that these cells are the lining cells in the lymphatic spaces, which under irritation, adopt a function which otherwise they do not possess. They become exceedingly large, wandering cells. The consensus of opinion is that they have very little to do with the destruction of microbes but their chief usefulness lies in the absorption of destroyed material. They are scavengers and I have advanced recently the idea, why ectopic gestation cases do so remarkably well after operation. In spite of their depletion, it is extremely seldom that you see any peritonitis after these operations, due to the fact that the blood in the abdomen has evoked these cells to activity.

There is another interesting factor: that if you examine the lymphatic spaces of any part of the body after a blood transfusion you will find, depending upon whether the matching had been perfect or not, but more especially in those cases where the matching has not been perfect, a widespread calling out of these cells and I think that in that

reaction lies one of the great virtues of blood transfusion against infection. It is very interesting to know that the hormones evoke this reaction. It has been a question in my mind why during pregnancy these cells should be so active in the uterus, but we find them also in the broad ligaments.

DR. EMIL NOVAK, BALTIMORE, MD.—The work of Dr. Fluhmann may indicate the possible rôle of the hormones in the vascular phenomena of menstruation, concerning which so little is as yet known. In our own studies of the human endometrium, we have been struck with the massive infiltration of leucocytes and large mononuclear wandering cells into the endometrium just before menstruation. This infiltration is apparently analogous to that which Dr. Fluhmann has observed in his experimental work. In the first half of the cycle the endometrium is quite clear of infiltration cells, but just before the beginning of menstrual desquamation the infiltration is so intense that, if one is not familiar with its normality, the picture would suggest a marked inflammatory process.

Presumably this phenomena is due to the cumulative effect of progestin, but its significance is not clear. When it is better understood, and when we know more about the effects of the sex hormones upon the blood vessels of the endometrium, we shall have taken a great step toward a clearer understanding not only of normal menstruation, but of such menstrual disorders as functional bleeding. I have always felt that the latter is not to be explained on the basis of simple tissue loss as a result of localized areas of thrombosis and necrosis, according to Schroeder's ideas, but that there must be some fundamental change in the permeability of the blood vessels themselves in order to explain the extreme hemorrhage so often seen in these cases.

DR. FLUHMAN (closing).—I should like to emphasize the point that it cannot be correctly stated that the hormones directly stimulate the reticuloendothelial system. On the basis of these experiments the only thing we can say is that the appearance of these cells is apparently an indirect effect. The hormones stimulate tissue growth and a local increase of blood vessels and as a result the tissues acquire the power of responding to trauma very much more readily with macrophages.

**Reconstruction of the Oviducts: An Improved Technic With Report of Cases, Drs. Frederick C. Holden and Francis W. Sovak, New York City. (Paper read by Dr. Sovak.) (See page 684, November issue.)**

#### DISCUSSION

DR. JAMES E. KING, BUFFALO, N. Y.—The problem of absolute sterility belongs clearly within the realm of surgery. The attitude of any surgeon toward such operations will depend somewhat upon what he may consider to be the criterion of success. Since the Rubin insufflation one's success may be judged by two criteria: first, the permanent patency of the tubes; and, secondly, the number of pregnancies which result from any procedure. In the past, results were judged entirely by the number of pregnancies that followed surgery and as the percentage of successes measured in this way was extremely low, it is not surprising that many of us have been rather cold toward tubal reconstruction. The Rubin insufflation, however, will give, I am sure, a new impetus to this type of surgery, and we now may have the two criteria of success, the persistent patency and the number of pregnancies which follow in a given series.

Dr. Sovak and Dr. Holden have taken as their own yardstick of success the permanent patency following operation. In this they were clearly justified because their operations were done in cases which were indicated for other reasons and they very frankly state that the procedures were done in their series for the purpose of developing the technic of the new procedure. The discussion therefore upon this paper focuses upon the procedures themselves. I have had no experience with the Bonney cuff operation, for I have always chosen in those cases of distal occlusion to split the end of the tube

and evert the membrane. It seems to me that, theoretically at least, that offers a little better chance because of the larger ostium which it affords. It would have been very interesting to me if they had commented upon the condition of the ovaries in their cases for certainly ovaries which require dissection to free their adhesions are in a condition which would make them likely to have new adhesions form with any new peritoneal contacts. Such ovaries in themselves might prevent normal follicle rupture.

The interest centers, of course, around this new procedure of implantation. I think very few of us have been enthusiastic about implantations of the tubes as has been formerly proposed, especially those ectopic implantations where the tube was placed somewhere outside of its normal position. The most important step, I should feel, in the implantation operation is the reaming out of the interstitial portion of the tube. Certainly this gives a wide lumen or opening for the implanted tube and such contractions as might occur as a result of the operative procedure or by contractions of the uterine muscle would not be sufficient to close or constrict the tube.

In one case in which both procedures were done, implantation and circumcision of the tube, and which was followed by pregnancy, I should call a real achievement. In my experience I have found that the cases of nodosa salpingitis are almost always associated with a distal occlusion and that would make it necessary, it seems to me, in many cases to do both of these procedures.

The value of insufflation in sterility operations is important in accomplishing three things: the first in diagnosis; the second in maintaining patency; and the third in determining the future condition of the tubes. I am personally a convert to Dr. Sampson's theory of endometrial implantation and I am just wondering whether in insufflation so early after operation there is not a possibility, theoretically at least, of pushing through endometrial cells that may find a site for implantation.

If success is based alone upon the number of pregnancies I think we may be privileged to take a stand as to what success means. Personally I feel that any procedure that will reclaim a very small proportion of a considerable number of these unfortunate women who are despairing and hopeless in their barrenness, justifies surgery. If these gentlemen themselves had taken as the standard for their success the number of pregnancies that followed in their series they might have done so with great credit to themselves. I think they have shown an unusual number of successes.

DR. EDWARD H. RICHARDSON, BALTIMORE, MD.—It was inevitable, of course, following the advent and development of tubal insufflation and hysterosalpingography that attention should sooner or later become riveted upon devising practical methods for restoring function to occluded tubes. Unfortunately I cannot add anything to this report from personal experience because I have never done a tubal implantation. However, a brief summary of the literature may be worth while, since Dr. Sovak did not have time to present one.

It is noteworthy that this operation was first done by an American surgeon, Thomas J. Watkins, who in 1897 first performed a tubal implantation in a woman from whom the other tube had previously been removed. The operation was followed by pregnancy which terminated in abortion. Another American gynecologist, Dr. T. S. Cullen, in October, 1919, performed the second operation of this type and achieved the first successful result on record. He implanted the outer portion of a patient's only tube after resection of the cornual end. Pregnancy occurred ten months later and was terminated by abortion. A second pregnancy occurred, however, which went to term and produced a normal child in June, 1922.

In addition to this report of Dr. Sovak's, I have collected from the recent literature reports of 58 tubal implantations. It is interesting that no American gynecologist is included in this group since the original reports of Dr. Watkins and Dr. Cullen. This contribution, therefore, is particularly timely and creditable to its authors. The ultimate result in most of these 58 cases is not ascertainable from the reports. However,

7 full-term pregnancies, 1 premature birth, 1 abortion and 1 tubal pregnancy, are known to have resulted. Undoubtedly this percentage of success is too high because many failures have doubtless never been reported. It is significant that no report has been made of a normal pregnancy following implantation where a salpingostomy was done at the same time. Heuck reports one tubal pregnancy which occurred under these conditions, and some authors very strongly condemn implantation where the other end of the tube is occluded, believing that there are other factors involved besides mere tubal patency. They interpret hydrosalpinx as indicative of permanent damage both to the tubal musculature, causing impaired peristalsis, and also to the cilia of the epithelium both of which results seriously interfere with the progress of the ovum through the tube and, therefore, predispose to ectopic pregnancy.

The indications for the operation are (1) occlusion of the uterine end of the tube by removable tumors; (2) tubal pregnancy in the uterine end; (3) nodular salpingitis; (4) congenital occlusion of the uterine end; (5) accidental section of the tube during some other operation; and (6) reconstruction following previous sterilization by ligation and division of the tube.

The technic of the operation as described in the literature is interesting in comparison with the method we have heard described today. The weight of evidence favors the cornua as the choice location. Preference varies, however, between the linear, the sagittal incision, and a trephine or reaming operation. Both Kiparsky and Sellheim have devised special trephine instruments which differ in some respects from this one of Dr. Sovak's. In all cases followed by pregnancy either a sagittal section or a cuneiform resection was done. Success has followed both splitting and nonsplitting of the implanted tubal end, but the majority of authors recommend splitting.

Just a word in closing about salpingostomy without implantation. A recent tabulation by Schmitz of Chicago of 371 cases reported by 13 authors showed 31 subsequent pregnancies, 8.36 per cent success. While a little apart from the operation we are considering today, this is a closely related subject. Naturally, salpingostomy is worthless unless patency of the tubes is at the same time established by means of retrograde insufflation.

DR. HARRY DORMAN, BAYREUTH, SYRIA.—In the country where I practice, in the Near East, a large majority of the gynecologic practice is due to sterility.

The first case that I opened at the fimbriated end conceived within six months and has since had three children though she had been married seven years before without having a child. She had had an abortion followed by occlusion of the tube. I have done altogether probably ten or twelve implantation operations, following very much the method described by Dr. Sovak, except that I did not have his reaming instrument. In the first case of implantation I had the beginner's luck and the woman had two children.

There is also the question as to whether the thickening of the tubes has interfered with peristalsis and whether the change in the mucous membrane also interferes with the passage of the ovum and conception. One thing I have noted is that the occlusion at the fimbriated end and occlusion at the isthmus are not merely the question of a different operation, but it also involves the change in the mucous membrane. The tube may be closed at the fimbriated end and the mucous membrane of the tube be fairly intact, but when you have an occlusion at the inner third it means a more serious lesion of the mucous membrane of the tube. When I take out a section of the tube from the isthmus I send it to the laboratory and ask them to show me the stricture.

DR. SOVAK, NEW YORK CITY (closing).—A woman has a peculiar psychologic make-up and wishes to be as nearly normal at all times as the other woman and will submit to any type of operative procedure to become normal. A woman with bilaterally diseased tubes, knowing that she has them, is also sick mentally, sometimes bordering on the psychopathic state, and even though you may not have pregnancy follow in all

cases, there is relief of the mental state and I think that should be considered in attempting reconstruction work.

In answer to Dr. King regarding the condition of the ovary, adhesions, etc., I think the heat treatment and suspension of the ovary overcome the congestion and relieve the inflammatory condition.

The early insufflation following operation is a fair criticism. We attempted to see how early we could do an insufflation test and, although we have had no morbidity following the attempt, we are not doing it as early as formerly.

In reply to Dr. Richardson and Dr. Dorman in reference to the damaged tube, we all know that a patient having had a virulent gonorrheal infection or a postabortal infection does become pregnant and there is no reason why a reconstructed damaged tube should not help in the production of pregnancy.

**The Relation of Placental Infarcts to Eclamptic Toxemia, A Clinical, Pathologic and Experimental Study, Dr. R. A. Bartholomew, Atlanta, Ga. (By invitation.) (See page 797.)**

DISCUSSION

DR. A. H. MORSE, NEW HAVEN, CONN.—Dr. Bartholomew's paper may be discussed from two angles. (1) The frequency of placental infarcts in the toxemias of pregnancy and (2) the effect of the injection into experimental animals of extracts of autolyzed placental tissue. Young has emphasized the possible relation of infarcts of the placenta to eclampsia. Young's theory holds that the presence of infarcts, even those which are ultramicroscopic in size, accounts for the clinical symptoms of toxemia. As is well known, the degenerative changes resulting from infarction form the most common abnormality of the placenta. However, from a gross and microscopic examination of some thousands of routine specimens I have never been convinced that the degree of infarction played a particular rôle in the causation of eclampsia. This viewpoint seems to be borne out by a roentgenographic study of placentae made in our clinic by Thoms. Thoms, after sectioning the injected and hardened organs measured the degree of infarction. Of three patients with definite toxic symptoms, the placenta in one case showed an infarction of 15 per cent; while in the other two no measurable lesion was present. On the other hand, ten patients who presented no symptoms of toxemia expelled placentae in which the percentage of infarction varied from 2 to 24. In any case, as Essen-Møller puts it, we still face the problem that all pregnant women carry placentae but that all do not have eclampsia. The fact that primiparae are more commonly afflicted than multiparae, might be explained by the fact that the latter gradually acquire an immunity. But here again we must explain why some primiparae escape.

The theory regarding the toxicity of broken-down cellular tissue recalls the deportation theory of Veit, the theory of Rosenau and Anderson, that eclampsia might represent an anaphylactic reaction and finally that of several German investigators who suggested that eclampsia depended upon the release into the circulation of placental endotoxines. Veit injected rabbits intraperitoneally with emulsions of placenta. This was followed by the appearance of albuminuria and sometimes by death. However, a similar stage is set when a tubal pregnancy ruptures and expels the ovum into the peritoneal cavity or when the placenta of a secondary abdominal pregnancy is left in situ at laparotomy. Yet in neither instance do symptoms of toxemia necessarily arise.

Murray and Johnstone who repeated Rosenau's work showed that while shock might be induced by the injection of extracts of autolyzed placenta, no similar reaction was induced when unautolyzed emulsions were employed. On the other hand they could reproduce toxic symptoms with extracts made from autolyzed liver.

I would therefore raise the question, whether the reaction on the part of the experimental animals would have been the same had the extracts of placenta been unautolyzed,

and also whether a reaction similar to the one reported by Dr. Bartholomew would not have been induced by the injection of an autolyzed extract of some other protein.

In considering the possible relation of abnormal placenta functions to the toxemias, we should not lose sight of the fact that during pregnancy there is a notable increase in the production of hormones. The human placenta contains folliculin and at least one other hormone which simulated that of the hypophysis. As Zondek has pointed out, this raises the question whether the placenta takes part in the production of hormones or whether it is only a resorption area for hormones produced in the hypophysis and in the ovary. In either case it is pertinent to ask whether a disturbance of this function by itself or associated with aberrations of other endocrine glands may not play a rôle in the toxemic manifestations in question.

Finally it is entirely logical to assume that abnormal placental functions play a part in the causation of the toxemias but fortunately it is exceedingly difficult to prove.

DR. JOHN R. FRASER, MONTREAL, CANADA.—It would seem that the most outstanding change brought forth in this work is the extensive degeneration apparently present in toxemia. However, if one undertakes an age period study of the changes in the placenta from the time of its development through to maturity, it is apparent even in the early stages of the placenta that degeneration is a physiologic change to some extent. We are familiar with the epithelial changes which appear after the fifth or sixth month. Then one is very much struck in the last three months of pregnancy with the frequency by which the degenerative phenomena appear. It would seem almost that this degeneration is a normal physiologic change in many placentas.

There are some very interesting changes in the placenta which one may find from time to time. For instance, in the chronic nephritic very marked degenerative changes are usually present. Then there is a small proportion of cases where the baby dies shortly before term in which an adequate explanation is not forthcoming, in which one may be able to show a rather diffuse degeneration which might be the cause of the unaccountable death.

Then one finds in some cases very extensive degeneration and not much evidence of toxemia. I have personally always looked upon the extensive changes which one sees in a chronic nephritis and in some forms of toxemia as perhaps being aggravated by the toxemia. That is to say, the degeneration which may be present to some extent is increased by the toxemia and I would rather perhaps put that interpretation upon it than, as some people do, for the cause of the toxemia.

The life history of the placenta is 280 days. Senility appears often prematurely in the placenta, as in other organs. It is natural, then, that toxic changes should influence such a physiologic change.

DR. BARTHOLOMEW (closing).—The work covered such a mass of data that it was very hard to present all the various facts in the time given but I must admit this, that in the first half of any such work when one is rather unfamiliar with the type of infarcts and has not classified them in his own mind as to etiology and types, the results will necessarily differ somewhat from those obtained in the last half of the work. We were first looking for infarcts that were definitely demarcated, and of a yellow or white color, not realizing the importance of the early infarcts that Young has so clearly described. In the last half of this work, and since the data have been collected, I believe that I cannot recall a single case of fulminant toxemia that has not shown this acute type of infarction. I believe that when the condition comes to be studied more in detail the types of infarction that I have just tried to emphasize, the acute and subacute lesions, will come to be recognized as quite a common finding in eclampsia.

As to the objection that the same lesions in experimental animals can be produced by extracts from other organs, I do not believe that is an objection. The poisons are common to any cellular tissue. We carried out the experiment of autolyzing human

liver, and obtained the same lesions in the kidneys and liver. Similar protein split products are produced, hence we obtain the same type of lesion in the liver and kidney.

While I do not, as yet, regard the work as an absolute proof that toxemia results from infarction of placenta, I do believe that it is the most fruitful and promising field for investigation and if this work will stimulate, in all clinics, the methodical examination of placentas, correlating the lesions and the symptomatology, I believe that it will be put on a firm footing.

**Increase in Guanidine Compounds in Eclampsia; An Experimental Study, Dr. Paul Titus, Pittsburgh, Pa. (By Invitation.) (See page 667, November issue.)**

DISCUSSION

DR. OTTO H. SCHWARZ, St. Louis, Mo.—Several years ago, Dieckmann, by injection of tissue fibrinogen intravenously and by feeding animals raw meat, was able to produce very extensive liver lesions, simulating the lesion of eclampsia, in many dogs. This work was presented before the New York Obstetrical Society.

I believe that the liver lesion in eclampsia is usually present, but it is not necessarily an accompaniment of the disease. The theory of the development of the lesion in my opinion, is as follows:

The ferments of the blood are concerned in neutralizing placental proteins as they enter the blood stream. From the intestinal tract are absorbed protein constituents more complex than amino acids in addition to amines which result from intestinal putrefaction. This absorbed protein material is not sufficiently neutralized, coagulation time of the blood is shortened in the portal system, and with the poisons that are absorbed, the endothelium can be readily damaged and coagulation with subsequent hemorrhage take place. I, therefore, think that no specific poison such as tyramine, histamine, or methyl guanidine is the toxic substance alone involved.

Methyl guanidine has been recently receiving some attention in the toxemias of pregnancy. Stander has recently reported on methyl guanidine in the blood of eclamptic patients and finds no increase. Grow and Senn did determinations of blood guanidine in some of our patients and in eclampsia they were able to confirm Standard's figures, but found guanidine markedly increased in one case of eclampsia, proven by autopsy, the patient having had no convulsions and was not in coma.

These workers also studied the blood in the early puerperium. On account of the profound changes in protein metabolism, they thought it might be of interest to study the guanidine content of the blood. Here also only normal values were obtained. To produce liver lesions similar to those in eclampsia, it seems to me that it would be rather difficult to do with substances as toxic as methyl guanidine. Some of the pictures which Dr. Titus has shown us, exhibit some damage. I would not say that the lesions are comparable with those found in eclampsia. In several of the slides, the lesions shown are not at all typical of the lesion in eclampsia.

DR. TITUS (closing).—I quite agree with Dr. Schwartz that some of the slides are not convincing, particularly because they were purposely selected to show merely the various stages in the familiar degenerative lesions of the liver as we developed them experimentally. The one showing the focal necroses is the most suggestive.

We have been strongly impressed by the similarity between the liver lesions produced artificially by Dieckmann, to which he refers, and those seen in eclampsia.

A problem which we are working on at present is an attempt to combine Dieckmann's ideas with ours by agreeing that the placenta is the reasonable source of his thromboplastin. To this end, therefore, we are now giving guanidine injections to pregnant guinea pigs because they have a placentation similar to human beings. We have already



noticed that the toxic and the lethal doses for these pregnant animals is considerably smaller than for nonpregnant ones, indicating that an increased susceptibility to this toxine is caused by pregnancy.

May I emphasize that this entire work which I have presented is still on an experimental basis.

**A Type of Pelvis Intimately Associated With Occipitoposterior Position, Dr. Herbert Thoms, New Haven, Conn. (Published elsewhere.)**

## OBSTETRICAL SOCIETY OF PHILADELPHIA

*MEETING OF MARCH 3, 1932*

DR. J. W. CUTLER presented (by invitation) **Artificial Pneumothorax and Pregnancy With the Report of Two Cases.** (See original article, page 914.)

DR. C. B. LULL presented **A Preliminary Report on the Use of Barbiturates With Ether by Rectum.** (See page 888 for original article.)

### DISCUSSION

DR. NORRIS W. VAUX.—I can unqualifiedly say that of all the analgesics, the barbiturates with ether have, after careful observation in a short series of cases, been most gratifying and successful in our hands. However, I do not believe it wise to use this method routinely. It is not at all good in the rapid deliveries of multiparae. The outstanding facts in these cases are as follows: (1) With the Gwathmey method we formerly had to wait until the labor was well established. With barbiturate ethyl that is not necessary. It does not seem to slow up the labor, which so often happened when we gave the Gwathmey analgesia too soon after the onset of labor. (2) With the cases under consideration we have observed that there has been no trouble with the establishment of the primary respiration of the newborn; whereas with the Gwathmey method we had difficulty with this complication. The infants seem to be born with a good color and a rather husky cry, even though ether has been added for low forceps delivery.

This preparation must be given by someone who is familiar with the technic of rectal analgesia. The patients remain in a condition of semicomma, but do not become entirely anesthetized. They are not able to coordinate or cooperate with the doctor in the second stage of labor.

DR. JOHN C. HIRST.—I wish to emphasize one addition to the advantages mentioned, namely the prolonged duration of Nembutal with ether, which obviates the unpleasant necessity of repetition as often experienced with the ordinary Gwathmey method.

In addition to the characteristic dry lips and flushing of the face from barbiturates, an occasional extremely rapid pulse rate will be encountered, which in two instances in my own experience has been quite alarming. Furthermore, one further precaution should be mentioned, that is the necessity for observing these patients after the birth of the baby as well as during labor.

DR. LULL (concluding).—I have not observed any rapidity of pulse in this series of cases as we did with sodium amytal.

DR. C. H. FRAZIER AND DR. HENRY F. ULRICH presented (by invitation) a paper entitled **Pathology of the Thyroid Gland Complicating Pregnancy**. (For original article see page 870.)

#### DISCUSSION

DR. PHILIP F. WILLIAMS.—We probably see fewer thyroid cases in this area than may be seen where endemic goiter is prevalent. But only about  $\frac{1}{2}$  of 1 per cent of these patients show symptoms of thyrotoxicosis during pregnancy.

I do not coincide entirely with the idea that pregnant women need iodine routinely as a part of prenatal care. I doubt very much if any of us feel that 10 per cent of our prenatal cases show sufficient hyperthyroidism to need this.

The more marked cases of hyperthyroidism stress the point which Dr. Frazier has brought up, i. e., that marked dysfunction of the thyroid gland is really no part of the pregnancy, it is a complication of pregnancy and should be handled by a thyroid surgeon. Basal metabolism alone may be misleading; it is the whole group of symptoms that must lead us to determine whether thyroidectomy is necessary. Any woman who shows severe symptoms should be seen by a thyroid specialist. Not all cases will have to have the gland removed. Probably not all cases will go through pregnancy, but certainly very few will have to have the pregnancy interrupted.

I have had three recent cases with marked thyroid disturbance. The first was a primipara, aged forty-four. She was anxious to have the child, having been sterile for a number of years. Her amenorrhea was thought to be due to a natural menopause but she was four months pregnant when I first saw her. She had a basal metabolism rate of seventy plus and a pulse rate of 144. With rest in bed and mild sedative treatment, but no iodine, she quieted down. Thyroidectomy was not considered for fear of a miscarriage, she went to term, had a ten-pound female child delivered by cesarean section on account of a breech presentation, and stood the anesthesia well, in spite of the thyroid condition. The symptoms became worse after the pregnancy and two years after the delivery a thyroidectomy was performed.

A second case, also a primipara, was one of marked exophthalmic goiter complicating pregnancy at term, she had had no rest, no treatment, no iodine during the pregnancy, and went through a normal labor. An operation was suggested but it was refused and she left the hospital in poor condition.

The third case had symptoms of a severe thyrotoxicosis. She received iodine 3 or 4 times during the five months of pregnancy during which she was observed, went through a normal labor, and showed marked improvement after delivery.

Two other cases were those of women upon whom thyroidectomy had been done. One went through 2 pregnancies without any disturbances and the other through one.

DR. EDWARD ROSE.—Several questions seem to me to be deserving of special mention:

1. The importance of the administration of iodine to pregnant women with and without goiter. An insufficiency of iodine may and often does result in the appearance of goiter and cretinism in the infant, even though the mother has had no apparent abnormality of the thyroid gland. This constitutes more of a problem in endemic goiter districts than in our own region. But it is a very simple and easy matter to assure the pregnant woman of an adequate supply of iodine simply by administering 10 mg., either in liquid or tablet form every week or two throughout her pregnancy. And since 50 mg. of iodine is sufficient to enable the adult thyroid gland to carry out its function during a year under normal circumstances one can easily make sure that both mother and infant have a good supply.

I believe that the routine administration of iodine to pregnant women is just as important a part of prenatal care as any other, and should be a part of all prenatal routine.

In cases where there may exist a simple, nontoxic, diffuse goiter, the dosage of iodine and the frequency of its administration should be increased somewhat. And even in the presence of hard or nodular nontoxic goiter, it is safe to administer iodine if it is done cautiously and the patient is kept under strict and frequent observation.

2. The tendency of pregnancy to be followed by an aggravation of preexistent simple goiter, or hyperthyroidism, or by the development of simple or toxic goiter is well known. In 635 cases at the University Hospital which Dr. Frazier and I analyzed in 1930, 9.9 per cent of the women with toxic goiter, stated that pregnancy immediately preceded the onset of their symptoms, or greatly increased them. I know that there is considerable difference of opinion on this subject, but I feel that pregnancy is a very important etiologic factor in both hyperthyroidism and simple goiter.

I am glad that the speakers refrained from assuming a dogmatic position on the necessity for or value of thyroidectomy in these cases. Here again there is a very great variety of opinion. It is generally true that most pregnant patients stand thyroidectomy very well, but any operation presents a threat to the continuation of pregnancy which cannot be ignored. I feel that discretion should be used in these cases and that a trial with iodine is often worth while. Even though the patient cannot be cured, she can often be carried along in a reduced state of toxicity and have the operation performed after labor.

DR. EDWARD A. SCHUMANN.—Until a short time ago surgeons have been reluctant to operate upon patients presenting evidences of acute thyroid toxemia during pregnancy.

There is one point to which I beg to direct attention, the occasional occurrence of rapidly developing symptoms of thyroid toxemia during pregnancy, which symptoms, whether treated or not, last perhaps a month or six weeks and then gradually decline in severity, disappearing after delivery. Patients suffering from this syndrome might readily be subjected to unnecessary thyroidectomy.

DR. FRAZIER (closing).—In the discussion on the relation of thyrotoxicosis to pregnancy one question has not been touched. For how long after an operation for the relief of thyrotoxicosis should the patient be cautioned against conception. In the patient already married or in the one contemplating matrimony our opinion is frequently sought and invariably we recommend an interval of at least a year. In those cases operated upon in the pregnant state we recommend an interval of two years.

In certain of the severe cases in our series that were operated upon during pregnancy, the induction of labor had been seriously considered. I do not believe that this should ever be considered as an appropriate way of managing a toxic thyroid during pregnancy or to put it another way, the principles underlying the treatment of toxic goiter during pregnancy differ in no respect from those in the nonpregnant state. Once the diagnosis is established it is safer for both mother and child to remove the toxic gland.

DR. B. C. HIRST AND DR. I. ANDRUSSIER presented a paper entitled **Uncomplicated Prolapse of the Ovary, Due to Elongation of the Infundibulopelvic Ligament, Its Treatment.** (For original article see page 879.)

#### DISCUSSION

DR. EDWARD A. SCHUMANN.—Penrose, Baldy and Beyea laid great stress upon this condition, regarding it as frequently congenital in origin, though often due to subinvolution of the uterus following pregnancy or abortion. The left ovary

seems to be more frequently affected than the right and a characteristic symptom is pain on defecation.

DR. G. M. LAWS read a paper entitled **Results of Operations for Prolapse of the Uterus and Bladder**. (For original article see page 864.) This was briefly discussed by Drs. J. H. Girvin and S. E. Tracy.

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## NEW YORK OBSTETRICAL SOCIETY

*MEETING OF FEBRUARY 9, 1932*

DR. CARL H. ILL, of Newark, N. J., presented (by invitation) **Two Cases of Pregnancy Following Watkins' Interposition Operation**.

Mrs. D., aged thirty-seven, was operated upon May 25, 1930, for a relaxed perineum, marked cystocele, and lacerated cervix. The cervix was amputated, and a typical Watkins' interposition operation done. Both tubes were doubly ligated, with linen thread, severed with cautery between the two ligations and stumps buried in the folds of the broad ligament. She also had a perineorrhaphy. She menstruated last on June 4, 1930, and was referred to me for delivery on January 4, 1931.

She had had three children; the first a long difficult labor, terminated by forceps.

She was never well after this, having painful menstruation headaches, backaches, and a feeling of everything dropping out of her vagina. These symptoms practically cleared up while she carried the other children. She felt well during this entire pregnancy, her only complaint being frequency of urination and burning at times. Examination when she came to me showed head high, but engaged in the pelvis, a long anterior vaginal wall, the scar of the interposition operation was very definitely felt. Blood pressure normal, urine negative except quite a few white cells.

On February 18 she came into the Hospital with slight pains. Abdominal examination showed back to the left, feet distinctly felt to the right; fetal heart rate 120, left lower quadrant. Pelvic examination showed head in midpelvis, pointing toward the rectum, anterior lip of cervix 10 cm. long. Diagnosis of left occiput posterior. Her pains soon stopped; castor oil and quinine were given the night of the twentieth followed by six 3 minim doses of pituitrin. At 10 A. M. on the twenty-first, vaginal examination showed head still in midpelvis, anterior lip of cervix 5 cm. long; cervix 5 fingers dilated. A sound was passed into the bladder, after catheterization, and was easily inserted for 6 inches. In fear of injury it was not passed any further, no obstruction being encountered. Caput was visible on February 22 at 4 A. M.; living child was easily delivered with low forceps in R.O.A. position.

After waiting one hour placenta was delivered manually. It was not thought advisable to use much force by Credé's method.

She reported on April 7 for follow-up. Perineum was somewhat relaxed, vagina subinvolved, and a slight erosion of the end of the cervix. Uterus small, antverted, no cystocele. She is now entirely well and has no pain at menstruation.

The second case, Mrs. S., aged twenty-nine, was referred to me September 4, 1931. She had had two children; the first after one hour's labor and the second after two pains. Both babies were said to have weighed over 10 pounds. In March, 1927, she was operated upon for a marked cystocele, rectocele, and lacerated cervix. The cervix was amputated, typical Watkins' interposition operation done, both tubes being doubly ligated with linen thread, severed with cautery between the ligation, and ends buried in the folds of the broad ligaments.

She menstruated last on February 15, 1931. Abdominal examination showed a hard, firm uterus, which was very definitely held down over the bladder region. Vaginal examination showed a very much elongated and thickened wall of the vagina, and the cervix was so far posterior that it could hardly be felt. She was very uncomfortable, had great difficulty in urination and had to be in bed most of the time. Her blood pressure was normal, urine showed considerable albumin, and 4+ pus. Her condition grew steadily worse, urinary symptoms increased, she had severe pains all through her abdomen. On October 19, 1931, a typical classical cesarean section was one, a living male child being delivered. On opening the abdomen the bladder was pulled way down under the pubes, and when the uterus was opened the anterior wall was 7 cm. thick. The posterior wall was extremely thin. The entire uterus had developed posteriorly, just as it so often does in a pregnancy following a ventral fixation. No opening into the uterus could be detected where the tubes had been cut. However, the location at both horns of the uterus were sewed over by redundant peritoneum.

She made an uneventful recovery and on her follow-up examination on January 4, 1932, showed perineum and cervix normal, uterus anteverted, small, no cystocele. Abdominal scar healed; patient has no discomfort.

In the first case the uterus developed normally and pulled the bladder up with it. Consequently, there was no obstruction and the baby was born normally. In the second case the uterus entirely developed posteriorly, causing a thick anterior portion, which almost entirely obstructed the birth canal, acting exactly like a fibroma which had developed in the lower anterior segment.

DR. O. PAUL HUMPHSTONE.—I have observed two patients who became pregnant after the Watkins' interposition operation. The most important point in these cases is whether or not the cervix is amputated. If the cervix is amputated in the interposition operation, the os will not dilate in labor.

DR. HARBECK HALSTEAD.—I have seen only one of these cases and we did a low-flap cesarean section because it was not possible to do anything else.

DR. ROBERT T. FRANK.—The thing that strikes me most is the question of the technic in sterilizing these patients at the time. In my own experience, which covers quite a large series of cases, probably over 500, I have noted only one pregnancy after ligation of the tubes. I lay great stress upon not peritonealizing these two transected ends in tying them with a single ligature, tying over the loop, first to one side and then to the other. I transect them with the scissors and take great care to see that the openings are parallel to each other and not peritonealized, because should reestablishment of the lumen occur the likelihood of the ovum finding the second entrance is much reduced. On the contrary, if a normal tube, just like a normal vas deferens, is buried after transection in a connective tissue sheath, the likelihood of reestablishment of continuity is greatly increased.

DR. ELIOT BISHOP.—The only thing I want to emphasize, as I have many times before, is that the actual sterilization is done by *peritonealization*, and not by artificial blocking. We have had no pregnancies follow this theory and practice of sterilization. About three years ago we collected over 100 cases and have had a number of additional cases since then. We cut off a loop of each tube over catgut ligature and leave the two ends parallel, as Dr. Frank mentioned. The ends slowly pull apart after peritonealization, which occurs in twenty-four to forty-eight hours. We have had the opportunity of opening two or three abdomens and have been able to demonstrate this.

DR. ALFRED C. BECK.—I recall some years ago treating a pregnant woman who had had an interposition operation and amputation of the cervix by Dr. Polak.

I do not recall whether he sterilized her or not; probably he did tie off the tubes. In that case I pulled a foot through the cervix, although it was very difficult to reach. Finally, the cervix dilated and a living child was delivered spontaneously by the breech.

DR. RALPH M. BEACH.—I would like to report a case of interposition during the childbearing period by Dr. Polak at the Jewish Hospital. At about the third or fourth month this woman developed a very marked elevation of the bladder, elongation of the urethra, marked clouding of the urine, distortion of the ureters, bilateral hydronephrosis, which was followed by retention, very marked toxemia, and jaundice. When she was brought to the hospital she was very sick. We emptied the uterus at this time, very easily, by an anterior hysterotomy. There being no bladder in front of the uterus, it was a very simple procedure. Following that the patient made a very rapid recovery.

DR. RALPH A. HURD.—Sterilization of women in the childbearing period when an interposition operation is done, should always be preceded by curetting. In my case the patient menstruated about the middle of May and I operated upon her in the Woman's Hospital the first week in June. I took great care to insure her against future pregnancies, but rather inadvertently neglected to curet the uterus. It seemed that she was pregnant at that time; she became pregnant between her last menstruation and her admission to the hospital, and she went on almost to term. I suspected a low implantation of the placenta, although I was never able to prove it on account of the great difficulty of examination. I did a cesarean section and she had a live baby five weeks from term. I think the sterilization has been well done because she has not become pregnant again.

The tubes were apparently occluded completely and the two cut ends were separated and closed, or peritonealized thoroughly. I had to make the incision way up on the fundus, practically on the posterior wall of the uterus. The bladder was drawn up to the top.

DR. BENJAMIN P. WATSON.—I believe that all of these complications could have been avoided had interposition not been done. I regard it as a bad operation.

DR. CARL H. ILL.—I did not operate originally on either one of these cases. They were referred to me for care during pregnancy. Both patients were Catholics, they would not consent to interruption of pregnancy, there was nothing else to do and, so, I had to let them go through with it. It so happened that both these cases were done by Edward III, and in going over his records with him I found that he has done almost 600 interposition operations. He has a very careful follow-up system and these are the only cases that he had that have ever become pregnant. He has used this method of sterilization, he tells me, for the last twenty years.

DR. JOHN J. MADDEN (by invitation) read a paper entitled **The Rôle of Calcium and Viosterol in Pregnancy.**

DR. VICTOR JOHN HARDING AND DR. H. B. VAN WYCK, of Toronto, Ont., (by invitation) presented a paper entitled **Researches on the Toxemias of Later Pregnancy.** (For original article see page 820.)

#### DISCUSSION

DR. H. B. VAN WYCK.—One of the striking things about the toxemias of pregnancy has always seemed to me to be the extreme number of varying types with a certain common association, and I feel that that has been too little taken account of in all etiologic discussions. We see that factor, too, in the difficulty that has been

encountered in arriving at any satisfactory method of classification. This so-called classification, you would say, looks worse than ever; but it is no classification at all. It relieves us of the necessity of giving a name which immediately becomes a bone of contention in these variable conditions, and it focuses our attention on the actual tissue and chemical changes which we see in any individual case. I think that is a valuable point of view, as well as Dr. Harding's suggestion that the formation of some of these as yet unknown combinations may be a starting point for further investigation.

With regard to the dietetic factor, the second part of the paper, may I say that the results of these experiments show that the only dietetic factor is salt.

The third part of the paper is in harmony with the hypothesis of salt and water disturbance, inasmuch as it seems to explain the success that has met with so many apparently, at first, discordant methods of treatment. With all these treatments, based on a variety of ideas, there is a certain proportion of success to be met with, and this is further in support of the hypothesis. After all, in these conditions in which prophylaxis is of peculiar importance and is in all our hands of peculiar efficacy, the test of any hypothesis to explain these conditions will be, I think, borne out chiefly in the extent to which it places in our hands a prophylactic agent, and I can, speaking from experience assert that this hypothesis is of value. In the last five hundred obstetric patients I have kept careful weight records. I expect that they shall gain three or four pounds a month or less. When they exceed that limit I then consider it necessary to take further steps. This simply is closer prenatal supervision, rest, and salt restriction. I know the fallacy of attempting to estimate any prophylactic success from anybody's series or any number of cases. The only fact that I can state in this 500 is that out of that number there were no serious toxemias and only three in which hospitalization was necessary. It is rational, at any rate, and would seem to be in harmony with the hypothesis.

DR. W. W. HERRICK.—Dr. Harding's opinions about the nature of the late toxemias of pregnancy are very much in accord with my own. The abandonment of the attempt to find a single cause and the attempt to correlate these disturbances with general medical conditions, has for many years seemed to be most desirable.

Recognition that the liver, the kidney, the cardiovascular system, and the nervous system bear the brunt of the late toxemias of pregnancy and that the clinical study of these patients often brings to light underlying defects in these important organs is a point of view which the obstetrician is rapidly accepting.

We recognize latent or obvious nephritis and hypertensive cardiovascular disease as being very definitely related to these toxemias. Hepatic disability is less well defined. Its rôle awaits the development of satisfactory tests of hepatic function.

One point deserves special emphasis. The internist believes that he can differentiate chronic nephritis and essential hypertension or hypertensive cardiovascular disease. In obstetric circles there is still a tendency to consider these two conditions as one. Careful follow-up studies and the observation of the behavior of patients with essential hypertension in pregnancy reveals the great importance of cardiovascular disease as distinct from nephritis in the late toxemias of pregnancy.

I believe the etiology of these toxemias will be found in many instances bound up with that of hypertensive cardiovascular disease as at present recognized by the internist. The solution of this problem awaits added knowledge in physiology. Dr. Harding's studies are an important step in this direction.

## BROOKLYN GYNECOLOGICAL SOCIETY

MEETING OF APRIL 1, 1932

DR. GEORGE G. COCHRAN, JR., presented a paper on **Avertin Analgesia in Obstetrics**. (For original article see page 849.)

## DISCUSSION

DR. JOHN CASAGRANDE.—I have followed a number of cases under avertin analgesia, and have used it in five cesarean sections. I have used 80 mg. instead of 60, supplemented by gas and oxygen. In cesarean section the patients come out of the anesthetic in two or three hours after the operation, free from nausea or vomiting, and they certainly seem to recover a little better than they do with ether or other general anesthetics.

DR. COCHRAN.—The greatest number of doses I have given any one patient is three, and that was in a forty-eight-hour labor.

We have observed no excessive bleeding after cesarean section in which avertin has been used.

DR. BARTON C. HIRST read a paper entitled **Some Experiences in the Diagnosis and Treatment of Congenital Anomalies of the Female Genital Tract**. (For original article see page 843.)

## DISCUSSION

DR. ISIDOR C. RUBIN.—I believe the question of the formation of an artificial vagina resolves itself into a decision between two technics. One consists in utilizing the labia minora. I have had one experience with this which was most gratifying. The patient remained at the hospital seventeen days. I had an opportunity to examine the patient several years after operation and subsequent to marriage, and she had been having perfectly satisfactory coitus. Another procedure is the one devised by Frank and Geist. The end-result after their operation is most satisfactory and permanent. It requires considerable patience in planning the plastic and in carrying out the technic later. However, it requires a minimum of six weeks of hospitalization and longer in some cases.

Urethral coitus, which is occasionally encountered, appears to be satisfactory to such couples. The combination of anomalous conditions in the genital or urogenital sphere and remote organic anomalies is also well known.

DR. G. W. KOSMAK.—The field of genital deformities in the female is one of intense technical interest, and yet, it may be advisable in many cases to let well enough alone, because even the successful technical accomplishment of the restoration of the vaginal canal, so-called, may lead to a considerable degree of trouble later on. I doubt whether the restoration of an anatomic result is sufficient in most cases to make up for the lack of physiologic background, and I believe that is one point which many of our expert plastic operators have missed. While they may be able to restore anatomic details, they are not able to develop the physiologic background which is necessary in a case of that kind.

DR. ERNEST D. RESNIK.—I would like to report a case of a patient twenty-two years old, who gave a history of amenorrhea of ten weeks' duration. She was admitted to the hospital with a diagnosis of incomplete abortion. Examination rectally showed an apparently normal uterus on the right side, and on further examination a large mass was found on the left side, the size of a four and a half months' pregnancy. Further inspection revealed a complete duplication of the uterus cervix and vagina. On speculum examination the right small uterus had a small piece of placenta protruding through the cervix indicating a pregnancy and abortion on the right side, and the uterus on the left side was still carrying the pregnancy at about four and a half months.



# Department of Reviews and Abstracts

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CONDUCTED BY HUGO EHRENFEST, M.D., ASSOCIATE EDITOR

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## Selected Abstracts

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### Abortion

Grann-Petersen: Treatment of Abortion. Ugesk. f. laeger 92: 837, 1930.

This report is based on 1118 actively treated cases of abortion out of 1146 hospitalized cases. The gross mortality was 0.61 per cent while that of the actively treated cases was 0.45 per cent. The afebrile cases numbered 747 and these were treated without mortality while in 371 febrile cases the mortality was 1.35 per cent. The incidence of genital complications following operation was 1.21 per cent in the afebrile and 3.5 per cent in the febrile cases.

After a review of these cases and some of the current literature on the subject the author concludes that the *one* indication for operative treatment (curettage) is an abortion which is already under way but that such conditions as ectopic gestation, induced abortion, complete abortion, salpingitis, parametritis and peritonitis must first be ruled out. Hemorrhage and infection are usually best avoided by early emptying of the uterus whether the case is febrile or not. In the later months of pregnancy, expectancy may be practiced and, in the presence of genital complications, interference is contraindicated. The treatment must be individualized as no rules will fit all cases.

The author subscribes to the following indications for emptying of the uterus as promulgated by Prof. Leopold Meyer: a widely dilated cervix through which the gestation products are easily passed; strong hemorrhage or exsanguination from a previous hemorrhage; and a febrile postabortal convalescence or foul smelling postabortal discharge.

REUBEN L. LARSEN.

Reichelt, H.: The Treatment of Abortion During the Last Ten Years. Monatschr. f. Geburtsh. u. Gynäk. 84: 357, 1930.

From 1919 to 1929, there were 1,870 cases of abortion at the Breslau Woman's clinic. The treatment of these cases was neither entirely active, nor entirely expectant. The usual treatment was that of "the middle line therapy." In cases where no fever was present, cervix patulous and adnexa normal, an immediate curettement was performed. If the cervix was closed, quinine was administered. Of the 674 afebrile cases 85.6 per cent were discharged cured, 14.3 per cent left the hospital improved and 0.1 per cent died. In 1,196 cases fever was present. Of these 82.2 per cent were treated actively, 6.9 per cent expectantly and 10.9 per cent conservatively. Among the 1,196 cases, 74.1 per cent were cured, 22.1 per cent were improved and 3.8 per cent died. Of all the 1,870 cases, 82.5 per cent were cured, 14.3 per cent were improved and 3.2 per cent died. The chief causes of death in the 60 fatal cases were sepsis (19), peritonitis (11), grippe (6), embolus (5), poisoning (4), purulent endometritis (4) and pneumonia (3).

Twice as many unmarried girls have abortions as married women and in contrast to the latter, the number of abortions decreases among the unmarried girls as their

age increases. In the entire series of cases, 5.9 per cent were therapeutic abortions, 11.3 per cent had definite causes, 10.7 per cent were distinctly criminal and 72 per cent were presumably criminal.

J. P. GREENHILL.

Olow, J.: Some Views on the Treatment of Miscarriages. *Acta obst. et gynec. Scandinav.* 9: 399, 1930.

The author favors active treatment of abortions for febrile as well as afebrile cases. In his series of 740 cases 300 had fever. The only exceptions to active therapy are ectopic pregnancy, imminent abortion, completed abortion, and the presence of salpingitis, parametritis and peritonitis. The treatment was entirely expectant in 107 cases, immediate operation in 351 and operation after expectancy in 282. There were 3 deaths in the series, one due to embolus and two to peritonitis. All were subjected to expectant treatment. The morbidity was very low.

J. P. GREENHILL.

Nahmmacher: Charcoal in Abortions. *Therap. d. Gegenw.* 10: 452, 1930.

The intrauterine use of charcoal is of marked value as a prophylactic measure in afebrile abortion and as a therapeutic agent in febrile abortion. The method is free from danger, simple to carry out and most rapid in its action. It is therefore a procedure which is available and practical for the general practitioner. The use of charcoal is indicated in afebrile abortion, febrile abortion, puerperal endometritis and cesarean section when done after the rupture of the membranes.

The technic of the introduction of the charcoal is very simple. The vagina is irrigated, the cervix grasped and two to four pencil shaped pieces of charcoal are introduced directly into the uterine cavity. The author does not believe in the mechanical dilatation of the cervix but always awaits spontaneous dilatation. Immediately upon the introduction of the charcoal a crackling sound is heard followed by the appearance of the foam. The cervical canal is then lightly packed with iodoform gauze for two to three hours. After that the charcoal is no longer active.

The author has treated 152 cases of abortion without charcoal and 122 with charcoal. His results in the charcoal series were markedly better both with febrile and afebrile cases. He was also able to improve his results in puerperal endometritis by the use of charcoal, especially in those patients in whom a cesarean section had been done after rupture of the membranes.

RALPH A. REIS.

Otto, Karl: Experiences With the Non-Operative Termination of Pregnancy by Means of "Interruptin." *Zentralbl. für Gynäk.* 56: 112, 1932.

"Interruptin" is a mixture of iodine and thymol in a fatty base. The author reports its use in twenty-four cases of pregnancy between 2 and 5 lunar months over a period of one year. Complete emptying of the uterus occurred at the conclusion of pains in only 4 cases, and in 2 cases there was bleeding of between 700 to 800 c.c. Twenty-three of the cases were afebrile during the puerperal course, and the other case ran only a slight temperature. Operative removal of part of the uterine contents by curettage was necessary in 15 cases.

WILLIAM F. MENGERT.

Engelmann, F.: The Danger of "Interruptin." *Zentralbl. für Gynäk.* 56: 119, 1932.

The author has collected from literature about 250 cases in which "Interruptin" has been used to terminate pregnancy and in that number has found 5 fatalities. Three of these were due to emboli, either fat or air, and the cause of the other two deaths was not ascertained.

WILLIAM F. MENGERT.

Lindqvist, E.: *The Abortions in Malmo, 1897-1928.* Acta obst. et gynec. Scandinav. 12: 306, 1932.

The case histories of 2,235 cases of abortion and more than 25,000 deliveries at the Malmo General Hospital from 1897 to 1928, inclusive, have been carefully studied by Lindqvist with regard to a number of different conditions, and subjected to statistic compilation and investigation.

The number of living children born to each 1,000 women between the ages of 17 and 45 has decreased in Malmo, the legitimate births falling from 245 in 1908 to 90 in 1927, and the illegitimate ones from 52 in 1908 to 19 in 1927.

The number of abortions registered annually in Malmo has risen from 121 in 1910 to 282 in 1927.

A previous pregnancy or abortion does not in itself appear to create any predisposition to genuinely spontaneous miscarriage in a later pregnancy.

A study of the frequency of abortion in different groups of married and unmarried women, especially as compared with the frequency of abortion in married primiparas suggests that there is extensive criminal abortion in all the groups except that of married primiparas.

The following approximate percentages of the total miscarriages in the last few years were due to criminal abortion: 10 per cent in married primiparas, 50 per cent in married secundiparas, 80 to 90 per cent in married tertiparas and multiparas and in unmarried women.

The percentage of repeated abortion rapidly increases in proportion to the number of previous pregnancies; among sextiparas, 48 per cent had aborted before, and of these 18 per cent had done so more than once.

Genuine spontaneous abortion probably appears more commonly after the end of the third month of pregnancy than earlier.

Unmarried women have apparently been practicing criminal abortion at an earlier stage of pregnancy the last few years than previously.

The frequency of febrile abortions was about 21 per cent in married women, and about 26 per cent in unmarried ones.

Of the total number of abortions at the hospital, 1.2 per cent terminated in death. Most of the deaths occurring among patients with septic abortion were probably due to criminal measures.

The mortality from abortion was as follows: For the afebrile cases 0 per cent. For the febrile cases with a rectal temperature between 38° and 38.5° C., 2.3 to 5.9 per cent and for the febrile cases with a rectal temperature of 38.5° C., or more, 5 to 13 per cent.

J. P. GREENHILL.

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### Erratum

In the discussion by Dr. Arthur H. Curtis on Dr. W. T. Dannreuther's paper, page 781 of the November issue, an error has occurred in the third line of the first paragraph. The latter should read as follows: "Consideration must be given to the age which a patient shall have attained before she is a fit subject for radium treatment of a nonmalignant condition" not a malignant condition.

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